FACTORS ASSOCIATED WITH ADHERENCE TO ANTIRETROVIRAL THERAPY

A Pilot Study conducted in the Western Cape, South Africa

Graeme Hendricks
HNDGRA002

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ABSTRACT

This study aimed to identify the barriers to and facilitators of adherence to antiretroviral therapy and attempts to understand these factors within a developing country context. A further aim is to add to the literature on antiretroviral adherence in South Africa.

Questionnaires were distributed to 42 participants at seven sites in the Western Cape where it was known that people were taking antiretroviral medication.

The study found overall that the adherence to antiretroviral therapy was facilitated by the knowledge of how the medication worked and the belief in the consequences of missing medication. However, the use of this factor within a developing country to improve adherence, raises other issues that need investigation. A barrier to adherence was the depression experienced by some of the participants in this study. A further finding that could indicate a trend was that black families were more involved in helping patients remember their medications than white families. It is suggested that more research is needed to develop adherence models that are appropriate and fit a developing country context.

Chapter 1: Introduction

This preliminary study is designed to investigate the factors associated with adherence to antiretroviral therapy (ART). Research on adherence to ART medication issues in South Africa, or in any developing country, takes place within contexts that differ from those in the developed world. This research is thus located within a socio-political context, a context of infrastructural issues as well as stigmatization of AIDS (Acquired Immunity Deficiency Syndrome). Although some of these issues are investigated in relation to adherence, the main focus of this study is more on the personal issues surrounding pill taking. These contextual issues in relation to the delivery of treatment in a developing country such as South Africa will, however, be considered.

Between 4 and 4.7 million South Africans are infected with Human Immunodeficiency Virus (HIV) (Garnier, 2001; Love Life, 2001). Prevention strategies must be an important element in South Africa's approach to the rate of infection whilst another part of the strategy and spectrum of care is the supply of ART. Research conducted both in South Africa and in other countries around the world has demonstrated the efficacy of ART in the form of "drug cocktails" in the treatment of people infected with HIV. ART " drug cocktails" can consist of three kinds of drugs, each targeting the virus at different stages of its life cycle: non-nucleoside reverse transcriptase inhibitors (NNRTIs) and nucleoside analogues reverse transcriptase inhibitors (NRTIs) which both prevent the infected cells from converting RNA into DNA, and protease inhibitors (PIs) which prevent HIV from being released from infected CD4 cells (Panos Institute, 2000). Highly Active Antiretroviral Therapy (HAART) is a dual or triple combination of two antiretrovirals and one PI (Mistry, 2001).

HAART has been shown to reduce the viral load to almost undetectable levels which means that the patients can live longer and have healthier lives (Volberding, 1999 in Tsasis, 2001; Orrell, Bekker & Wood, 2001). In South Africa in 2000 it was estimated that 20 000 individuals were on ART (Bredell Consensus Statement, 2001), mainly

through clinical trials and people who work for large companies who have subsidized medication (Simmons, 2002; Schoofs, 2002).

Concerns expressed both internationally via the Harvard Consensus statement (2001), and within the South African government circles, were that people in a resource poor country like South Africa would find it difficult to take antiretroviral drugs consistently. The debate in this country has been so contentious that it has led to both a High Court and a Constitutional Court ruling instructing government to supply at least mono-therapy (one antiretroviral drug) to pregnant women. The supply, however, of combination therapy or HAART is going to occur in a pilot site in Guguletu, Cape Town (Smetherham, 2002). A further site is being planned for Johannesburg (Personal Communication, Mcintyre, May 18, 2002). Given the fact that at least 20 000 people with HIV/AIDS are taking ART this study is warranted. Furthermore, the plan to distribute ART via the public health system, makes studies like these even more imperative.

The debate about whether resource poor countries such as countries in Africa, Asia and South America can deal with HAART is ongoing. HIV/AIDS related costs could be divided into direct and indirect costs (Panos Institute, 2000). Direct costs are the costs involved in tests for HIV and other diagnostic tests, treatment and prophylaxis for opportunistic infections, including visits to the doctors and hospital stays and antiretrovirals. Indirect costs are the costs involved in physical and technical infrastructure (buildings and medical staff), which are shared with other aspects of health care.

In the northern hemisphere antiretrovirals are funded mainly by governments or private companies, whereas in the southern hemisphere very few countries can afford to subsidise, to a greater or lesser extent, the costs of these drugs. At present, Brazil, Senegal, India and Thailand are supporting the costs of antiretrovirals and the different governments have invoked various strategies in order to deal with the costs of the drugs. Brazil and India have been manufacturing generic antiretrovirals by using a loophole in international law. Senegal, however, has set up a multisectoral approach with France to deal with the distribution of antiretrovirals in that country (McGeary, 2001; Panos Institute, 2000; Delaporte, Desclaux, Mselatti, Taverne &

Vidal et al., 2001). The South African government has consistently stated their concerns about the affordability of the drugs.

The issue of infrastructure within developing countries has been a concern in that the countries hardest hit by HIV/AIDS, are those countries which have the lowest number of medical personnel, especially in the rural areas where the majority of Africans and Asian live (Panos Institute, 2000). Other infrastructure issues include access to clean water, electricity, medical facilities routinely running out of basics such as painkillers, and poorly equipped clinics. In a developing country context it has been demonstrated that interruptions in antiretroviral adherence were not only due to the patients' inability to adhere, but was also due to financial in-affordability of the drugs and insufficient stock (Souteyrand, 2001).

Another argument against the issuing of ART to people in resource poor countries in Africa and elsewhere is that the person on these regimens needs to understand the concept of taking pills at a particular time and with certain foods. USAID head, Andrew Natsios is reported to have said in an interview that, with the high level of illiteracy in Africa, he doubted whether people could tell time and therefore would not be able to take their medication on time. This statement has been agreed to by some, most notably South Africa's minister of health, and been deemed racist by others, such as Frommer (2001).

Despite all the skepticism regarding whether or not resource poor countries can deal with HAART, some success stories have emerged in some countries such as Brazil with its dedicated HIV/AIDS clinics and high adherence rates, Senegal, Botswana, the HAART- DOTS (directly observed therapy) programme in Haiti and the success of a trial done in Cape Town. These reports have demonstrated that people in African and other developing countries people can adhere as much, or better than, people in the developed world (Farmer, 2001; Mbewu, 2001; Medrum, 2001; Orrell et al., 2001; Pablos- Mendez, 2001). The question therefore whether adequate adherence can be attained in a developing context has been answered. Although rates of adherence have been researched and reported on, virtually no published articles exist about what factors, besides those mentioned already, promote or impede adherence. But, cognizance has to be taken that adherence is still a worldwide issue and as is also

stated in the DHHS guidelines cited as an authority by the CDC in Atlanta: "imperfect adherence is common in the United states" (Frommer, 2001). Also contrary to Natsios' views that African patients will have particular problems is the statement that within America clinicians are reminded that factors such as "gender, race, socio-economic status, educational level, and past history of drug use" do not reliably predict poor adherence." Conversely, according to Frommer (2001), as reported in an article in JAMA 1998, a high educational level and high socio- economic status does not predict adequate adherence.

Stigma is a major obstacle in most developing countries. A study from Brazil reported that although "the type of therapeutic may have had some bearing on patient adherence, life style adaptation and problems related to stigma of the disease were actually more important" (Melchior, Nemes, Jordan, Okasaki & Komatsu, 2000). Stigma is also an issue that has also been raised in relation to access to treatment in Africa and elsewhere. It was reported by Ezama (2001) that in Uganda many people including the wealthy and well-educated sectors of the population presented with late stage HIV disease. The time of the presentation according to Ezama (2001) was related to the effects of stigma. In South Africa, Govender, McIntyre, Grimwood & Maartens (2000) reported that people travel away from their homes and attend clinics elsewhere because of perceived stigma attached to HIV. Mann (1990) pointed out that health care workers (HCW's) responses followed a pattern of initially not wanting to work in the HIV/AIDS field because of the stigma attached to AIDS. Although no direct studies have been done in South Africa on the care delivered to HIV/AIDS patients, what has been noted in other countries is that doctors and nurses could perceive these patients as being less deserving of care (McCann, 1999). Lengner (2002) stated that, in the sample of nurses interviewed at a psychiatric hospital in South Africa, many participants exhibited strong feelings of "revulsion" towards HIV/AIDS patients.

In essence, the context within which this study occurs, is that the South African government does not appear to support the mass distribution of antiretrovirals, because of the costs involved, both direct and indirect, the perception that the high levels of illiteracy will interfere with people's ability to adhere to the regimens and the stigmatization that still exists in developing countries such as South Africa. These

concerns need to be balanced by evidence from the developing world as well as the one published study in South Africa (Orrel et al., 2001) that people can maintain a high adherence rate and the acknowledgement that in South Africa increasing numbers of people are taking ART.

Pilot studies of patients' perceived barriers and facilitators to ART are needed, because although adherence rates had been studied in the Orrell et al. (2001) study, that study was not designed to look at barriers and facilitators and the only barrier noted was the complexity of the regimen the patients were on.

The structure of this thesis is as follows: Chapter 2 is a review of the literature organized around patient related, regimen related, clinician related and disease related factors. The international literature is summarized and literature relating to tuberculosis medication is considered with a view to identifying barriers and facilitators to adherence. The single reported study on adherence in Cape Town is discussed. A rationale for the present study is considered. In Chapter 3 the quantitative methodology is discussed, the research tool and the changes made is discussed as well as a motivation for the use of self-report in adherence studies. In this chapter the data handling and statistical analysis as well as possible limitations are discussed. Chapter 4 provides the descriptive statistics as well as the results from the correlations and regression analysis. In Chapter 5 the findings are discussed and placed within a South African context. Limitations of this study are offered and suggestions for future research are made.

Chapter 2: Literature Review

A review of the recent literature on AIDS and related issues was conducted by searching the electronic journals section of the Internet using the words AIDS, antiretrovirals and adherence, and by scanning the relevant journals. A major source of information was the review article by Tsasis (2001). By cross-referencing the bibliographies of the different articles, seminal articles started to emerge. These articles were gathered as far as possible via the Internet as well as ordering them via the library. Library searches and collection of articles occurred between February 2002 and May 2002. Other sources from which articles were gathered were the abstract CDs from the Durban 2000 International AIDS conference. These articles and poster session presentations were requested via e-mail. The major bodies of work investigated in relation to adherence were mainly drawn from developed countries such as the USA, UK and countries on the European continent. It should be noted that thus far only one article (Orrell et al., 2001) on adherence to antiretroviral medication has been published in an academic journal in South Africa.

It is important to point out that although the literature refers to adherence and compliance, compliance according to Williams (2001) suggests "obedience to health care professionals", whereas adherence suggests a more collaborative effort between the health care professional and patient in ensuring success in taking medication. For this reason the term adherence is used in this study. Adherence as reviewed in this section concerns the factors associated with adherence and non-adherence to pill taking regimes. A lesser amount of literature is about adherence to other medical recommendations such as medical appointments, nutritional or pharmacological counseling, other rehabilitation programs such as alcohol or drug counseling or other service utilization such as physiotherapy etc., which may all be part of the spectrum of care offered to HIV positive individuals.

Adherence to medications has long been a focus of study (Rabkin & Chesney, 1998). It has been estimated that non-adherence to prescribed medications in the general population ranges from 10 to 92% with an average incidence of 50% (Eraker et al., 1984 in Singh & Squier, 1996). Research conducted on the use of other chronic

medications has shown that such medication is difficult to take and only about 50% of people do take them (Eraker et al., 1984 in Singh & Squier, 1996). According to the Hopkins Report adherence follows a J shaped curve with 50% of patients taking medication over 80% of the time, 20% taking medication 50-80% of the time, and 30% taking medication less than 50% of the time (Eldred & Cheever, 1998).

Similar figures of 20- 80% non-adherence to medications other than antiretrovirals was quoted by Williams (2001). It has also been estimated that the incidence of non-adherence among patients with chronic illnesses is even higher (Haynes, 1979 in Singh & Squier, 1996). An important difference between other chronic medications, such as hypertension and diabetes medication, and antiretrovirals is that if patients on the aforementioned regimens only take half their medication and then improve their adherence, they will still receive the full benefit of the medication (Williams, 2001). However, with antiretroviral medication, besides the lack of reinforcement, such as immediate tangible benefits, the future effectiveness of this medication and even of those in a related class of antiretroviral medication will be compromised if adherence is not maintained (Bamberger et al., 2000b; Catz, Kelly, Bogart, Benotsch & McAuliffe, 2000; Williams, 2001). Therefore, studying the adherence rates and reasons for adherence and non- adherence of persons taking combination antiretroviral therapy becomes important, as 95% adherence has a significant impact on the virus (Paterson, 1999 in Ostrop & Gill, 2000; Tuldra et al., 2000). In the Tuldra et al. (2000) study it was noted that adherence was high for the first few months but declined over one year. A further impetus for studying the factors affecting adherence and non-adherence is the fact that non-adherence has both dire consequences for the individual, such as the development of resistant strains of the virus, and the possibility that these could be passed to others in the community during high risk activities. This transmission of these multi-drug resistant strains could potentially pose a public health risk (Bamberger et al., 2000b; Hecht et al., 1998 in Catz et al., 2000; Wainberg & Friedland, 1998).

Adherence to ART has thus become an important focus of study and has been studied extensively searching for variables or factors that are correlated to adherence. Although these factors have been sought by a number of researchers it has to be remembered that adherence as stated before could be not only about the act of taking

prescribed medications (Kennedy, 2000), but is also about changes in nutritional health status and having to change diets, keeping medical appointments to check efficacy of drug regimens, other medical conditions that may arise or medical conditions that the person has had before and mental health status such as depression (Dunbar, 1993 in Kennedy, 2000; Haynes et al., 1979, O' Hanrayan, 1981 in Tsasis, 2001).

Adherence is not just about taking a pill but is a multidimensional process. This process includes a patient and his/ her specific characteristics such as the past history of adherence, social support, history of substance use, knowledge of the disease, or pre-existing illnesses. Adherence would depend on the type of treatment received, which includes such specific characteristics of the medication such as the type of medications, the duration the person would need to take it, frequency, complexity of the regimens, inconvenience, efficacy of medication and side effects. Environmental factors would impact on this process with specific characteristics such as scheduling, confidentiality, a comprehensive program that could include home visits or follow-up such as telephone calls and the location or incentive offered such as enablers, for example, food parcels or money. Another factor is that the disease (HIV/AIDS) has characteristics such as chronicity, symptomatic status, cultural norms attached to it, as well as education or health status. The providers of health care also have an impact and it depends on whether they are specialized, what level of HIV/AIDS training they are exposed to, sensitivity or personal beliefs about HIV/AIDS, as well as patient-provider factors such as the relationship and communication that exists between them and what type of reinforcement is supplied for adherence (Kennedy, 2000). A way of organizing the factors or variables that affect adherence is one offered by Tsasis (2001) in four broad areas or categories, namely "patient related", "regimen related", "clinician related" and "disease related" factors. The rest of the review will use these categories or factors as an organizing principle to explore the impact these factors have on adherence. Although this organization is used it should be noted that the factors interact dynamically with each other.

2.1. Patient related factors

2.1.1. Demographics:

Demographic factors have been used in the search for predictors of adherence. The most common factors that have been investigated include age, levels of education, race, sex, socio-economic status and occupation. Overall adherence does not seem to be predicted by gender, race, education level or occupation (Frommer, 2001; Griffith, 1990, Lopez-Saurez, 1998 in Tsasis, 2001). Support for the contention that demographics are not good predictors of adherence was offered by Pratt et al. (2001) in their study in which age, social class, ethnicity and level of education were not associated with adherence. Another study found that variables such as marital status and personality factors also did not consistently predict adherence (Meichenbaum & Turk in Rabkin & Chesney, 1998). Specific demographic factors are discussed below.

a. Age:

Although some studies have shown that a younger age may predict poorer adherence, in other studies no such an association has been shown (Pratt et al., 2001; Holzemer, 1999, Roca, 2000 in Williams, 2001). Gordillo, del Amo, Soriano & Gonzalec- Lahoc (1999) in a study in Spain found that younger people tended to have poorer adherence rates than older individuals. A possible explanation for this difference in findings was that in the Gordillo et al. study almost 44% of the study population were intravenous drug users (IVDU). Their findings may have been influenced in that the younger population in their study may have had a larger proportion of drug users. However, it was found that adolescents did present with some difficulties with regards to adherence and only 41% reported adherence (Murphy, Durako, Muenz & Belzer, 2001; Rogers, Miller, Murphy, Tanney & Fortune, 2001). But as was pointed out in the Rogers et al. study, anecdotal evidence pointed to the fact that adolescents' pill taking behaviour was affected by the presence of friends. Thus although a younger age might be a factor, it was influenced by other factors such as possible greater drug usage and the developmental stage adolescents are in. Therefore although overall it would seem that that younger people may have greater difficulties, with adherence it might be contingent on other factors.

b. Education level:

Adherence does not correlate with educational level (Gordillo et al., 1999; Pratt et al., 2001; Williams, 2001). Kalichman, Ramachandran & Catz (1999), although finding that education level was not predictive of adherence, did find that literacy was important to long-term adherence. They further qualified this by saying that literacy and educational levels were not necessarily related to health literacy. Kalichman et al. (1999) also stressed that health literacy, a more specific index of understanding medical instructions, was important to adherence. It has, however, been shown that people with low literacy levels use more health care resources (Kefalides, 1999). It appears then that educational level was not a good predictor of whether people could follow a regimen or not. Low literacy could affect long-term adherence as well as being a drain on resources.

c. Sex

Most studies in the northern hemisphere have been done on men (Tsasis, 2001). This is partly due to the profile of the disease in America and other countries where drug trials have occurred (Panos Institute, 2000). Some studies have shown that women may be at risk for non-adherence (Williams, 2001). However, others have found no such an association (Holzemer, 1999, Roca, 2000 in Williams, 2001). It was possible however, that women with dependent children adhered better than men (Tsasis, 2001). This review will not cover adherence among women on short courses to prevent mother-to-child transmission of the HI virus. No difference in adherence was noted in women from different races in the review performed by Johnston Roberts & Mann in 2000. A study conducted by Johnston Roberts (2000) dealing with women and keeping journals over a period of a month, revealed that although the prediction of adherence may not be through gender, women do face obstacles such as being care-givers to children, being too busy, subject to issues of social relationships and putting on weight. Women also, according to this study, were worried about wasting and had difficulty taking the ART on an empty stomach. Another barrier was taking pills in public and risking exposure of their HIV status. (Johnston Roberts, 2000; Johnston Roberts & Mann, 2000). Taking pills in public is not only a concern for women, however, but also for adolescents (Murphy et al., 2001). This is supported and explained by Rogers et al. (2001) reporting that since stigma to HIV still persists in communities, taking medication regularly and consistently means that the patient may inadvertently be exposing themselves, with attendant fears of social and economic

reprisals. A further reason for non-adherence supplied by the participants in the Johnston Roberts (2000) study was that if people were away from their own environments they did not consider it to be "safe" to take medication.

For men, non-adherence also has some association with working outside of home and the connection was that patients became too busy to take their medication (Chesney et al., 2000; Johnston Roberts, 2000; Johnston Roberts & Mann, 2000; Kennedy, 2000). Supporting evidence of this factor was gained from a study in which it was reported that when people, both male and female, are away from home they have to remember to take their medications with them (Hecht, 1998 in Chesney et al., 2000; Johnston Roberts, 2000).

Sex therefore may not be a predictor, but the actions the different sexes engage in during the day need to be considered, as well as the more sex associated concerns such as putting on weight and safety aspects of exposure of women's HIV status.

d. Socio-economic factors

Socio-economic factors include income, household income, occupation, employment status and housing status. Different studies have used these as markers of the socio-economic status of the participants of the various studies. Williams (2001) in a review of adherence studies states that adherence does not correlate with income. Although Kleeberger et al. (2001) found that socio-economic factors "significantly discriminated lower adherence," the lower income referred to in this study was above the middle income in the general population. Therefore, according to the authors, this difference could be attributed to other factors. In the 1999 study by Gordillo et al., being employed was revealed in first level analysis as a predictive factor for adherence. Further analysis, however, revealed that being employed did not make much difference. Socio-economic problems such as homelessness, substance abuse and alcoholism were listed as factors affecting adherence (Smith, 1996, O'Brien, 1996, Weidle, 1998 in Tsasis, 2001). Evidence on adherence rates among the "marginalized, substance users and poor" have been mixed. According to Bamberger et al. (2000b), some studies have shown that adherence among marginalised housed, i.e. people living in sub-economic housing and homeless populations is not markedly different to other groups of HIV positive individuals. Bangsberg et al. (2001)

supported this position. There are, however, practical issues that may affect adherence among the homeless, such as storage of medications and having food available with certain medications (Bamberger et al., 2000).

There is still considerable debate about the use of demographic variables in the predictions of adherence. It does not appear, however, that demographics are a consistently good predictor of adherence. Although age seemed to influence adherence, it was contingent on other factors such as possible drug usage or developmental stage. Educational level was also not a good predictor although it does appear that health literacy may be a better predictor. Sex on its own was not a predictor, but looking at the different concerns such as safety aspects of taking medication in public and weight gain or loss may help the patient more with adherence. It appears that all socio-economic groups experienced difficulties with adherence, with the lower income group being exposed to more practical difficulties that have to be taken into account if adequate adherence is to occur.

2.1.2. Mood and other psychiatric disorders

Although psychiatric states are discussed in this section, the main focus is on depression, a factor that has been included in many studies thus far. It must, however, be remembered that when authors have referred to depression it could mean both the affective mood state of feeling sad and the more psychiatric definition of depression measured by instruments such as the Beck Depression Inventory (Rabkin & Chesney, 1998). Depression has long been associated with immune suppression and other health outcomes in studies on individuals with and without chronic diseases (Ikovics et al., 2001).

In general, research findings indicate that non-adherence seems to be associated with "psychological distress, emotional disturbance, depression and poor adaptive coping" (Singh & Squier, 1996, p 5). Rogers et al. (2001), although only from anecdotal evidence, speculates that the degree to which adolescents accepted their HIV status plays a key role to initiating therapy and particularly long-term adherence. This does, however, demonstrate that the distress and the disturbance caused by the diagnosis and the resulting depression, and an inability to cope with the diagnosis, could all affect the ability to adhere to antiretrovirals. Murphy et al. (2001) also reported in a

study on an adolescent cohort that higher levels of depression were significantly related to decreased adherence. Broers (1994) in Singh & Squier (1996) reported that a study conducted in Switzerland among psychiatric patients found lower rates of adherence although the nature of the psychiatric difficulties was not specified. Besides depression it was found that other psychiatric conditions such as schizophrenia and paranoia affected adherence (Haynes et al., 1979, in Tsasis 2001; Kennedy, 2000).

A study on the extent to which a psychosocial factor such as depression contributed to adherence with regards to AZT found that depression did affect adherence (Chesney et al., 1996 in Catz et al., 2000). Gordillo et al. (1999) found that depressed individuals adhere worse than non-depressed individuals, irrespective of the social support they have. The design of the study did not lend itself to establish a causal link between depression and poor adherence (Gordillo et al., 1999). Catz et al. (2000) found that depression and severity of side effects influenced adherence. It has been suggested that depression with its associated features of self-neglect, lack of motivation and forgetfulness could affect pill-taking behaviour (Kleeberger et al., 2001). This also might explain why, if depression is affecting the motivational system, the patient may be less able to cope with the side effects.

Chesney & Folkman (1994, p164) go further by stating that besides a patient's previous psychiatric illnesses, the "psychological sequelae of HIV disease itself does include depression, anxiety, somatic complaints and suicide ideation" that could all affect adherence. In essence it would seem that both the psychiatric and more common understanding of depression affect adherence and should be noted in all patients with HIV/AIDS. Also acknowledged was that psychiatric patients with other illnesses would pose a dilemma with regard to adherence to antiretroviral therapy.

It appears that whereas depression affects adherence behaviour, there is no certainty that it also causes an accelerated HIV disease progression. Some studies acknowledge that there might be a link (Lyketsos, 1996 in Gordillo et al., 1999) whereas others have claimed there is a definite link (Zorrilla, 1996, Burack, 1993 in Gordillo et al., 1999) with depression used as an indicator of shorter survival period in HIV positive men (Markowitz, 1994, Mayne, 1996 in Gordillo et al., 1999). Singh & Squier (1996) claimed in their study that depression was associated with greater declines in CD4

counts and a trend towards accelerated mortality. In the Kennedy (2000) review many articles cited depression as a major reason for non-adherence and patients ranked it as one of their most important reasons for not adhering. In a seven-year longitudinal study of HIV positive women conducted by Ikovics et al. (2001), it was demonstrated that depressive symptoms are associated with disease progression and more negative outcomes.

It appears therefore that depression not only affects adherence negatively, but also interferes with perceptions of social support, motivational systems, as well as having a negative impact on disease progression.

2.1.3. Knowledge of and Beliefs about AIDS and Treatment

a. Education about HIV/AIDS (disease) and adherence

It was reported by Eldred (1997) in Tsasis (2001) that the patient's knowledge of his or her diagnosis, including the purpose of the medication regimen influenced adherence. Williams (2001) in her paper also commented that patients who understood how their medications worked to help them were more likely to adhere to their regimens. In another study it was found that although knowledge of the illness and belief in the treatment was high, it was not associated with adherence (Gordillo et al., 1999). This may, however, be an anomaly due to the particular study population that included a high percentage of IVDU users that may have affected the results.

b. Self-efficacy:

The belief and the intentions that a person holds about a particular behaviour influence that behaviour. However, the gap between intention and actual behaviour, in this case adherence to medication, needs to be explored (Sweeney et al., 1998 in Gordillo et al., 1999; Strecher in Glanz, Lewis & Rimer (ed), 1997). With regard to adherence to medication, exposure to the side effects may influence that belief. This point will be discussed further under side effects (2.2.1).

Adherence appears to be associated with a patient's belief that they can follow a particular medication regimen, the belief about actual or perceived side effects of the medication as well as the perceived benefits of the treatment. All of these beliefs are

influenced by the beliefs about taking medication in general (Tsasis, 2001). Perceived self-efficacy as a variable is useful according to Tuldra et al. (2000) in that it related to high levels of adherence one year after beginning ART. Self-efficacy refers to the ability to take the medications and patients who were non-adherent had lower self-efficacy (Chesney et al., 2000; Johnston Roberts, 2000; Tuldra et al., 2000). Catz et al. (2000) in their study found that perceived self-efficacy to adhere to antiretroviral regimens was related to adherence. Eldred (1998), in Catz et al. (2000), noted that patients' beliefs about their ability to adhere even with mono-therapy (with AZT, zidovudine) appeared to be related to higher levels of treatment adherence. Johnston Roberts (2000, p. 162) found that persons who had made a decision based on an "active, thoughtful and informed decision" to take ART, had adhered to the regimen thus demonstrating their self-efficacy.

c. Treatment Efficacy

The belief in the treatment offered, known as treatment efficacy, in relation to affecting illness outcome, could be associated with adherence. (Samet, 1992, Samuels et al., 1990 and Besch, 1995 in Tsasis, 2001). It was found that with mono-therapy, skepticism around the efficacy of AZT affected adherence (Muma et al., 1995 in Singh & Squier, 1996). Besides demonstrating a lower self-efficacy, non-adherent patients also demonstrated a lower perceived efficacy of treatment benefits or medications they were using (Bamberger et al., 2000b). Also stated in Johnston Roberts & Mann (2000) was that women who did not believe in the efficacy of the drugs had problems with adherence. In a study done with patients it was found that if patients believed in the efficacy of the medication, they took the medication despite the side effects (Johnston Roberts, 2000). Gordillo et al., (1999) however found no association between belief in the treatment and adherence.

To sum up it appears that a person's belief in self, as well as a belief in the treatment they are taking supports adherence despite the side effects of the medication. Chesney et al. (2000) suggested that training and counselling patients prior to initiating combination therapy could be worthwhile in fostering beliefs in treatment efficacy. It is also reported by Williams (2001) that using reports or graphs that demonstrate the medications' impact is a powerful motivating tool for continued adherence. This is supported by Johnston Roberts (2000). The patients can see the effects of the

medication on the viral load, especially if the patient was asymptomatic before starting treatment (further discussion under characteristics of the disease 2.4.2).

2.1.4. Alcohol and drug usage

Non-adherence and alcohol consumption is correlated in the Chesney et al. study (2000) and support for this assertion that alcohol consumption could affect adherence is found in Bamberger et al., (2000b). Kennedy (2000) in his review found that non-adherence was an issue for patients who actively used recreational drugs. The idea that when people take recreational drugs, they are likely to be non-adherent is supported by Pratt et al. (2001). However, some people who use drugs beyond the recreational stage, i.e. people with drug addictions, can adhere to demanding regimens (Bangsberg et al., 2001 in Williams, 2001; Rabkin & Chesney, 1998). This further demonstrates that although factors that could impede adherence must be noted, they are not exclusionary.

2.1.5. Influence of other medical conditions:

Kennedy (2000) in a review found that if HIV was not the only medical condition, this affected adherence as the person involved was taking other medication. Williams (2001) confirmed that very often ART medication was not the only medication patients were taking as they were often also on other medication regimes such as those for opportunistic infections. It is thus important to be aware of patients on multiple medications, given the possible interactions between the drugs.

2.1.6. Common reasons for not taking ART

One of the main patient-related characteristics for non-adherence and reasons why doses are skipped is that patients simply forget or sleep through doses and are busy with other things (Kennedy, 2000). Some patients, however, used reminders and cues, and according to Kemppainen, Levine, Mistal & Schmidgall (2001), this strategy was used more by patients over 50 years old. Patients who used the fact that medication interfered with their lifestyles as a reason to not adhere, were recommended to use planning as a means to facilitate adherence (Kemppainen et al., 2001). It has, however, been noted that the extent to which the regimen interferes with the patient's daily life affects the adherence (Bamberger et al., 2000b; Johnston Roberts & Mann, 2000). Johnston Roberts (2000) found that patients who "routinized" their pill-taking

by integrating it into their daily routines were more successful at adherence. This was particularly successful with people who had predictable daily schedules. Ostrop & Gill (2000) found that adherence could be improved by providing patients with adherence aids and devices that counteracted forgetfulness.

2.1.7. Social Support:

A factor that has been investigated in many studies in relation to adherence to ART and the high rates of adherence needed to maintain viral suppression is social support, which although seen and dealt with in this section as a patient factor, can also be viewed as an environmental factor.

Social support has been demonstrated to buffer the impact of a wide variety of stressful life events including illness. Research has shown that people with illnesses such as malignancy, coronary artery disease and other medical conditions have with social support adapted better to the crises of illness, and demonstrated less anxiety, depression and somatic complaints (Bruhn et al., 1984 in Swindells et al., 1999). Three types of support, namely emotional, tangible and informational can be recognized and therefore social support can be different for different people at various stages of the disease. If it is informational and tangible support that is needed, then emotional support may not be satisfying, and if new symptoms arise then informational support may be needed (Swindells et al., 1999). In most studies the type of support needed at any stage of the disease was, however, not considered and many studies focused only on the perceived emotional support offered by friends, families and by clinicians.

A lack of social support has been shown to predict non-adherence to antiretroviral medication (Catz et al., 2000; Chesney et al., 1996; Spire et al., 2002). Catz et al. (2000) cite a study by Mostashari (1998) that showed that good emotional support aids adherence. Patients therefore who perceived less emotional support, and those who were less confident of their ability to adhere, were most likely to report inconsistent use of HAART (Catz et al., 2000). A cautionary note from Catz et al. (2000) was that it was difficult to say whether this relationship was causal. Other researchers have found that it is important for adherence that patients have supportive significant others who also understand and agree with the treatment regimen

(Johnston Roberts, 2000; Besch, 1995, Eldred, 1997 in Tsasis, 2001; Williams, 2001). An example where tangible support may play a role is that one of the major reasons for non-adherence is that no one reminded the patient to take their medication (Kennedy, 2000; Sarason et al., 1988 in Murphy et al., 2001). Patients that adhere to medication also report greater social and emotional support from their health care providers and significant others (Singh & Squier, 1994; Morse, 1991 in Tsasis, 2001). It was found by Kemppainen et al. (2001, p. 125) in a study in the USA that certain "patients groups most influenced by positive support from health care providers, family and friends included non-white patients, patients under the age of 50 and patients with fewer years of education." This study concluded that social support was needed less by older people than younger people. In another study it appeared as if older people were less satisfied with the social support and were using more maladaptive coping strategies, as well as being more vulnerable to social isolation (Swindells et al., 1999). In a study done in the UK, living alone was seen as a factor that affected non-adherence (Pratt et al., 2001). Social support according to Johnston Roberts (2000) meant more than just reminding patients to take their pills and also included cooking the correct foods and refilling prescriptions. Furthermore it was also stated in this study that social support could mean that the patient "modeled" the adherence behaviour of friends. There appears to be overall agreement that social support is important for adherence to ART but that it sometimes needs to be tailored to what the person needs at the time.

Social support is once again not a factor that can be considered in isolation as it would depend for example on whether the person was open about their HIV status so that they could access support, or whether depression was interfering with the patients ability to perceive and accept such support. Furthermore according to Gordillo et al. (1999, p 1768), social support "does not contribute further to adherence in the presence of depression." Social support nevertheless appears to be an important factor to consider irrespective of age, with the proviso that it needs to be specific to what is being requested.

2.1.8. Summary of patient related factors

Conclusions that can be drawn from the literature thus far are that socio-demographics are not good predictors of adherence. Age, sex, education level and socio-economic

status all seem to have contingent factors that influence adherence. Depression affects adherence negatively and appears to impact negatively on disease progression. In many studies forgetfulness and sleeping through doses have been common reasons for not adhering. In order to adhere, it appears that people with AIDS had to have a knowledge of AIDS and needed to know how their treatment worked. In addition, people had to believe that they could adhere to the regimens they were on. A facilitator of adherence was if people believed in the treatment and received visual feedback about the effects of their treatment. Alcohol and drug usage appear to affect adherence negatively, but they should be seen as factors that impede adherence rather than be used as exclusionary factors. It also appears that if people with AIDS had other medical conditions and were using medication, this factor could influence their adherence to ART. Finally, social support appears to be an important factor for adherence and needs to be specifically tailored to the patient's needs.

2.2. Regimen related factors:

Regimen related factors include side effects, dietary requirements, complexity of treatment and drug holidays.

2.2.1. Side effects

Antiretroviral medications are extremely difficult to take and can cause a number of unpleasant side effects due to their toxicity (Grahame-Smith, 1998; Kemppainen et al., 2001; Kennedy, 2000; Ungvarski, 1997 in Johnston Roberts & Mann, 2000; Orrell et al., 2001) Patients therefore need to understand the medication side effects to better prepare them for their onset (Kennedy, 2000). It was also found that addressing drug related concerns with patients was important for adherence (Tseng, 1998 in Ostrop & Gill, 2000). Williams (2001) goes further by stating that it was important not only to foster the patients' understanding of the side effects but also to teach patients how to manage them, and that these interventions had significant effects on adherence. It would appear according to Boyle (2000) that side effects are overtaking other reasons such as dietary restrictions and complexity of regimens for non-adherence. Patients are less prepared, at least in the northern hemisphere, to accept enormous discomfort, caused by the pills, unlike when HAART first appeared.

2.2.2. Dietary requirements

With ART, food requirements can sometimes be complicated as some medications have to be taken with fatty food, some without fatty food, others on an empty stomach, some with water and others without water (Gallant & Block, 1998; Johnston Roberts, 2000). Johnston Roberts (2000) found that socio-economic issues could play a role here in that patients with a lower socio-economic status may not always have the necessary dietary resources to be able to adhere fully as some medications are dependent on these foods for optimal efficacy. Dietary studies in cardiovascular disease demonstrate that "the more regular a patient's diet the better for long-term compliance to a restricted diet" (Metz et al., in Gallant & Block, 1998, p. 7). Simpler regimens in the form of simpler dietary requirements could aid adherence (Gallant & Block, 1998).

2.2.3. Complexity and dosing requirements

The more complicated the medication regimen is, the more difficult it is for the patient to take it (Bailey et al., 1995 in Murphy et al., 2001; Williams, 2001). Johnston Roberts (2000, p 159) also stated "the sheer magnitude of the complexity of the regimens was too great for patients." It was also asserted that the complexity of regimens affected all patients regardless of education level or age (Bailey et al., 1995 in Murphy et al., 2001). Kleeberger et al. (2001) found that if the regimen contained more than three ART medications it was associated with lower adherence. Murphy et al. (2001), in his study of adolescents, reported that the number of medications that needed to be taken also influenced adherence. Another variable or factor that appears to influence the level of adherence is the frequency of dosing and not the number of tablets having to be taken at any one time (Singh & Squier, 1996). This debate about whether the dosing requirements influence adherence was addressed by Gallant & Block (1998) citing a literature review by Greenberg (1984), which found that once-daily and twice-daily dosing regimens had higher adherence than three and four times dosing. This is important support for the contention that adherence is affected by the number of daily dosing rather than the amount of tablets at each dosing. In the Kemppainen et al. (2001) study the simplified regimens of twice-daily dosing seemed to have a positive impact on adherence. In South Africa, the Orrell et al. (2001) study supported this assertion. It is important that, as noted and reported by Catz et al. (2000), patients sometimes mentioned that when taking doses one was constantly

reminded that one was HIV positive and experienced the psychological impact of this reminder. It was also reported in the Johnston Roberts & Mann, (2000, p. 6) study that women felt that taking pills reminded them of the chronicity of the disease as well as pulling them out of "normality" and into "sickness." A common reason given by patients for non-adherence was the confusion over regimen requirements (Catz et al., 2000). Regimens then, according to Friedland (1997), where possible, should be made as simple as possible. This simplicity is also called for because AIDS patients are often on other medications as well as combination therapy (Kleeberger et al., 2001; Williams 2001). In a study based on a once daily dose of ART it was found that the regimen was well accepted, tolerated and the efficacy results were comparable to more complicated regimens, thus confirming that adherence is affected by the frequency of daily dosing and not by the number of tablets at each dose (Maggiolo et al., 2000).

2.2.4. Drug Holidays

Patients often take "drug holidays" which are defined as taking a little or no medication for three or more days (Johnston Roberts, 2000; Kennedy, 2000). Kleeberger et al., (2001) found that this was not virologically damaging if the patient was otherwise perfectly adherent, but the disruption in medication did have a huge effect on patients who already had lowered adherence. It has according to Katzenstein (1997) in Kleeberger et al. (2001) been shown that reducing medications versus stopping drugs may result in a higher rate of resistant mutations being produced. Patients therefore need to negotiate drug holidays with physicians and involve stopping rather than reducing intake.

2.2.5. Summary of Regimen related factors

It appears that the regimen related factors that affect adherence to ART include the side- effect profiles of the medication, the complexity of the dietary requirements and the complexity of the daily dosing regimens. It that twice-daily dosing is more effective than three-times daily dosing. "Drug holidays" did not necessarily have a negative effect if negotiated with the physician and that it involved stopping all drugs rather than reducing intake.

2.3. Clinician Related factors

2.3.1. Role of clinicians

Key roles for clinicians include supplying the patients with clear explanations for the use of their medications, encouragement, reassurance, support and sustained follow-up (Kennedy, 2000; Dimatteo et al., 1993, Roberts, 2000 in Tsasis, 2001). All of these factors would further enhance patient adherence (Davis et al., 1997, Chung et al., 1995 in Tsasis, 2001; Williams, 2001). It was found in Brazil that the health care skill at maintaining dialogue during the earliest stages of treatment was important for adherence (Melchior, Nemes, Jordan, Okasaki & Komatsu, 2000).

Gordillo et al., (1999) found that they could not demonstrate a correlation between the relationship between patient and provider and improved adherence. The study concluded, however, that it was not possible to discount that this in fact may be the case. From a more interpersonal perspective, Friedland (1997), discussed improving adherence through education around HIV, through involving patients in decision-making, assisting patients, simplifying regimens and maintaining a good relationship with the patient. In Kennedy's (2000) study on rating predictors of adherence, this decision-making was last on patients' lists about things that help them adhere. In the Johnston Roberts (2000) study, patients reported that physicians had motivated them to stay on their medication. Adherence is further influenced when the physician is available to answer questions, has a non-judgemental attitude, reinforces the treatment regimen, provides positive feedback, and assists the patient to incorporate the treatment regimens into lifestyle (McPherson- Baker et al., 2000; Davis et al., 1997, Chung et al., 1995, Roberts, 2000 in Tsasis, 2001). A factor found by Capozzolo et al. (2000) in Brazil was that the doctors were focusing solely on adherence to ART and not allowing patients any leeway to discuss their difficulties in living with the illness and with the treatment. With regard to interventions to improve adherence, Chesney et al. (1999) in Catz et al. (2000) suggests that patient provider communication could be improved.

In a study of health care providers it was pointed out that they often lacked the time, education and resources to prepare patients to begin combination therapy and to enhance adherence (Gerbert, Bronstone, Clanon, Abercrombie & Bangsberg, 2000;

Johnston Roberts & Volberding, 1999). They often just educated people and this may not be effective as knowledge alone does not impact on adherence (Cummings et al., 1982 in Gerbert et al., 2001; Prochaska et al., 1992). Given time constraints that physicians practice under, it may often mean that an interdisciplinary approach may be necessary. Many studies have shown that adherence is not just about taking medication, but is impacted upon by many other factors. It has also been stressed in many papers that listening to the patient as a whole is necessary if adherence is to be achieved (Capozzolo et al., 2000; Johnston Roberts, 2000; Tsasis, 2001).

2.3.2. Clinical monitoring

Fewer visits to physician's means less clinical monitoring and less frequent pill refills and lower adherence and thus may be a good marker for measurement (Kleeberger et al., 2001; Lucas, Chaisson & Moore, 1999).

2.3.3. Training of clinicians

Another factor that could influence treatment outcome is the lack of training that doctors have in understanding the complexities of adhering to complicated regimens (Ungvarski, 1998). It has been pointed out that in South Africa the lack of infrastructure and training in HIV medications may hamper adherence (Heywood, 2000). Issues around training were also mentioned by Boyle (2000), who concluded that many clinicians have not taken full advantage of the newer, less complex regimens available.

2.3.4. Summary of clinician related factors

Clinicians need to have non-judgemental attitudes, not only towards adherence issues but also towards other factors that impact on patients' lives. Further training needs to be ongoing to keep up with the latest developments in the pharmacological field so that simpler regimens could be prescribed.

2.4. Disease related factors

The chronic condition and unique characteristics of the AIDS syndrome have both been investigated with regard to their effects on adherence.

2.4.1. Chronicity of AIDS

The severity of the disease as well as its chronicity have been shown to influence adherence (Griffith, 1990, Gidran, 1998 in Tsasis, 2001). It has been shown with other chronic diseases that adherence to treatment decreases over the course of treatment (Hond, 1998 in Tsasis, 2001). With hypertension, half of those who begin treatment drop out within the first year, and of those who remain in care, only two thirds adhere to the correct medications (O' Brien et al., 1996 in Tsasis, 2001). HIV, because of its higher morbidity, has a higher adherence rate. This influence on adherence rates may be seen in the USA, where morbidity due to AIDS declined from 29.4 persons per 100 to 3.7 persons per 100 after the introduction of combination therapy (Pallela et al., 1998). It appears that the severity had a positive effect on adherence to medication for this chronic disease.

2.4.2. Characteristics of AIDS

The difficulty with HIV is that patients remain asymptomatic for years and this limits the perceived benefits from adherence to the regimen (Samet et al., 1992 in Tsasis, 2001). The side-effects of the medication are therefore often worse than the initial symptomotology. In a study by Singh & Squier (1996) it was found that having had a prior opportunistic infection was a positive predictor of adherence to medication and they concluded that asymptomatic individuals might perceive themselves as less vulnerable, and is thus less motivated to comply. This would be supported by the Health Belief model in that patients had learnt the costs and experienced the disease and thus would be further motivated to adhere to medications (Williams, 2001). Being symptomatic before treatment, according to Rogers et al. (2001), provides both positive and negative reinforcement when people skip doses with other chronic diseases. When people therefore skip doses with these diseases, each failure has consequences that can be learnt. With HIV, however, the long asymptomatic phase provides "no such incentive to initiate or adhere" (Rogers et al., 2001; Samet et al., 1992 in Tsasis, 2001, p 111).

2.4.3. Summary of disease related factors

Although the severity of the AIDS morbidity had a positive effect on adherence, the intersection with the characteristics of the disease, such as its largely asymptomatic initial presentation, had a negative effect on adherence.

2.5. Conclusions drawn from the international literature

Contrasting and sometimes contradictory results relating to most of the factors emerged from the various studies done in this area. No one factor can be used to successfully predict adherence, neither can any one group of people be singled who would find it particularly difficult to adhere.

Considerable debate still exists about the use of demographic variables in the predictions of adherence. It does not appear however that demographics are a consistently good predictor of adherence. Although age seemed to influence adherence it was contingent on other factors such as possible drug usage or developmental stage. Education level was also not a good predictor, although it does appear that health literacy may be a better predictor. Although sex on its own was not a predictor, looking at what concerned the different sexes may help the patient more with adherence. It appears that all socio-economic groups experienced difficulties with the lower income group being exposed to more practical difficulties with regard to adherence and these have to be taken into account if adequate adherence is to occur. Socio-demographics are therefore not good predictors of adherence. All socio-demographic variables seem to have contingent factors that influenced adherence. Depression affects adherence negatively and seems to impact negatively on disease progression. In many studies forgetfulness and sleeping through doses have been common reasons for not adhering. In order to adhere, it appeared that people with AIDS had to have knowledge of AIDS and needed to know how their treatment worked. People on ART had to believe that they could adhere to the regimens they were on. A facilitator of adherence was that people believed in the treatment and received visual feedback about the effects of their treatment. Alcohol and drug usage appear to affect adherence negatively but they should be seen as factors that may impede adherence and were not to be used as exclusionary factors. It also appears that if people with AIDS had other medical conditions and were using medication, then this factor could influence their adherence to ART.

Although social support is seen to be important, it is once again not a factor that can be considered in isolation since it would depend for example on whether the person was open about their HIV status so that they could access support, or whether depression was interfering with the patients ability to perceive and accept social support. Social support nevertheless appears to be an important factor to consider, irrespective of age and needs also to be specific to what was being requested by the patient.

It appears that the regimen related factors that affect adherence to ART include the side- effect profiles of the medication, the complexity of the dietary requirements and the complexity of the daily dosing regimens. It is also apparent that twice-daily dosing works better than three-times daily dosing. "Drug holidays" did not necessarily have a negative effect if negotiated with the physician and that it involved stopping all drugs rather than reducing intake.

Clinicians needed to have non-judgemental attitudes, not only towards adherence issues, but also towards other factors that impact on patients' lives. Further training needed to be ongoing to keep up with the latest developments in the pharmacological field so that simpler regimens could be prescribed.

Although the severity of the disease had a positive effect on adherence, the intersection with the characteristics of the disease such as its largely asymptomatic initial presentation had a negative effect on adherence.

All these factors can interact dynamically with each other. The adherence behaviour, therefore, of any patient is a unique experience of the individual intersection between all, or part of, the factors mentioned above. When dealing with adherence behaviour it is important not to locate it within an individual paradigm but rather be more comprehensive and include the complexity and characteristics of the regimen, clinician behaviour, as well as social and environmental factors.

International studies have moved beyond trying to predict, according to socio-demographics, which groups of people may have more difficulties than others with

adherence. These studies focus on what barriers and facilitators exist for individuals and communities in order to enhance adherence, given the high levels of adherence needed to maintain virologic suppression and immunologic resurgence. This move was also important because the ethics involved in refusing treatment purely on the grounds of the patient's demographics is debatable, even given the consequences of poor adherence (Tchetgen, Kaplan & Friedland, 2001). Studies also have been conducted with patients themselves as it has been shown that physicians overestimate adherence as well as seeing the barriers and facilitators to adherence differently to patients (Kennedy, 2000). Patients therefore needed to be researched for their perceptions of barriers and facilitators to taking antiretrovirals.

All the literature reports on studies performed in other countries and it is therefore necessary to look at the South African experience in relation to facilitators and barriers to adherence with other chronic medication. In South Africa the chronic disease tuberculosis (TB) has received attention because of the large numbers of people (24%) who have not completed their treatment (Assad, 2002). Adherence to TB medication has proved difficult in South Africa (Assad, 2002; Hansen, 2002; Simmons, 2002) and the factors that seem to influence adherence and have acted as barriers have been patient factors such as stigmatization, fear, treatment side-effects, time, poverty, substance use, use of traditional medicine, social mobility and external locus of control (Dick, 1998). Other influencing factors have been staff or clinician factors such as nurses being overwhelmed by numbers of patients, distancing barriers and neglecting the psychosocial aspects of the disease (Dick, 1998). Another group of variables that may be labeled clinic factors are that nurses are task oriented, that there is little continuity of care, little patient education and that follow-up is sporadic. The factors contributing to adherence to TB medication has been that clinics are oriented towards acute symptoms, that the focus is on symptoms and laboratory results and that the patients' role in their cure is not emphasized. This all leads to poor staff-patient relations and poor clinical outcome (Dick, 1998).

In Cape Town it has been demonstrated that urban dwellers of all races, socio economic groups, language and cultural groups can adhere to ART (Orrell et al., 2001). It was noted in this study that the barrier to ART was the complex nature of the regimens that influenced adherence. In this study, in terms of demographic

descriptors, male persons who spoke Xhosa were the poorest adherers (Orrell, Bekker & Wood, 2001b). However, what this study did not note was what other barriers and facilitators to taking medication there were. Considering what the international literature has stated, it could be speculated that the site used had well-qualified doctors with well-qualified counselors and that a supportive structure therefore was present at the site. Noted also in a commentary on this trial was that the languages in which people were cared for was mainly English and Afrikaans, and that it was possible that the people who did not adhere did not understand and were not educated about HIV and the consequences of not taking medication (TAC newsletter, 2002). Noted also was that the site was far away from where some people stayed which may have been a facilitator to adherence, since it has been noted in another study that people traveled far distances away from their homes if they were HIV positive, not wanting to be identified in their communities (Govender et al., 2000). However, these are all speculations as to what the barriers and facilitators are to taking ART in an urban setting.

2.6. Rationale of the study

Given the paucity of studies in South Africa and taking cognizance that predictors are not sought, a study on the barriers and facilitators to adherence to ART is needed. These facilitators and barriers should be sought using the organizing principles of patient, regimen, disease as well as social and physical environment related factors. This study therefore aimed to use the factors found in the international literature and the Adult AIDS Clinical Trials Group (AACTG) questionnaire to carry out a quantitative study in order to identify the major obstacles or barriers to adherence and to identify which factors gain significance as facilitators. These factors could include self- efficacy, belief in treatment, knowledge and beliefs surrounding skipping medications, social support issues, common reasons for not adhering, complexity of the drug regimen, depression, stress and alcohol/drug usage. The study would use the patients' responses not to predict adherence but to possibly suggest ways of overcoming barriers and enhancing facilitators. Support for this kind of study is offered by Delaporte et al., (2001) who state that taking into account the imposition ART has on people's lives, such as the special diets associated with the therapy and the timing of doses, it therefore becomes necessary to find the factors that either favour or hinder adherence to necessary procedures. The study therefore addresses the

following question: what are the factors that impede adherence and facilitate adherence in a sample of Western Cape People Living With HIV/AIDS (PLWHA) on antiretrovirals?

Chapter 3: Methodology

3.1. Introduction

The literature suggests that clear predictions of adherence to ART is difficult because of the interrelatedness of the different variables or factors. There exists few clear links between socio-demographic variables and adherence to ART. A greater link appears to exist between the presence of depression, social support and beliefs and knowledge about AIDS and ART and adherence. Although alcohol and drug usage impacts negatively on adherence they are not exclusionary factors. It appears as if side-effects and increasing complexity of regimens, especially if they require dosages more than twice-daily, have an effect on adherence. Having a well-trained and empathic doctor influences adherence positively and if patients perceive the severity of the disease, it also appears to impact on adherence. Although clear predictions do not seem possible, an option is therefore to study the factors that either facilitate or impede adherence in that these more often than not could be improved and thus improve adherence.

In South Africa the one published study (Orrell et al., 2001), noted that the complexity of the regimen was a barrier to adherence. It is therefore necessary to search for factors that load positively, i.e. aid adherence, and those which load negatively, i.e. impede adherence in the South African context. Although it is realised that 95% adherence is optimal for viral suppression, the reasons for non-adherence or skipped doses is more important for this study which is therefore not aimed at measuring adherence rates, but rather concentrates on the reasons why patients miss or do not miss dosages. The actual kinds of medicine being taken were regarded as being of lesser importance.

3.2. Study Design and Recruitment

The study was conducted on a sample of 42 HIV- infected women and men who are currently taking ART. These participants were recruited from seven sites in the Western Cape. Data was collected from July 2002 to the first week in August 2002. Sites that were known to have people taking HAART were telephoned and the head of the site was asked for permission to explain the purpose of the study and for permission to deliver the questionnaire via an indirect means to their patients/clients

so that the researcher would therefore not have direct access to the patients or clients and anonymity would thus be insured. No site that was approached refused access. A covering letter explained who the researcher was as well as the purpose of the study, guaranteeing not only strict confidentiality but that also the names of the sites would not be revealed (see appendix 1). A worker at each site would ask potential participants to take part in the study. Those willing to participate were handed the questionnaires that were self-administered. All the information divulged in the questionnaires was confidential and the completed questionnaires were handed back to the worker at the site. The participants were also promised that feedback to the sites would be via a report from all the participants so that the individual sites could not recognize which participants attended their sites.

3.3. Measurement Instrument

For this pilot study it was decided to use a tool designed and tested in the United States and which has been utilised extensively in other parts of the world (Personal Communication, Chesney, May 20, 2002). The questionnaire used comprised two parts and was designed by the Adult AIDS Clinical Trials Group (AACTG). It consisted of the baseline questionnaire (Baseline Correlates of Adherence) and the follow up questionnaire (Adherence to Antiretroviral Medications) (See appendix 2 and 3 respectively). As the researcher would only have a cross sectional view it was decided to combine the two.

The original questionnaires were developed by the Recruitment, Adherence and Retention Subcommittee of the Adult Outcomes Committee, and the Patient Care Committee of the AACTG. This group included social scientists, physicians, nurses and pharmacists. The original testing took place in 10 clinical trial sites and was self administered with staff being encouraged to assist patients when necessary. All 75 patients were on combination therapy, including at least one PI (protease inhibitor), and one or more NRTI or NNRTI. The instrument was delivered between May and June 1997.

Original instruments focused on recent adherence to maximize recall and minimise bias. Variables included were those known or hypothesized to affect adherence to medications such as alcohol and drug use, reasons to enroll on the trial, psychological

distress and adherence self efficacy (Dunbar- Jacob, 1990, 1993, in Chesney et al., 2000; Ikovics and Meisler, 1997 in Chesney et al., 2000; Wainberg and Friedland, 1998). Some of the questions in the original questionnaires were standardized scales.

Patients were also asked about more distal adherence, i.e. skipping medications over the past weekend and in the past month (Chesney et al., 2000). Patients who reported skipping medications were presented with a list of 14 reasons why people were missing their medications and were asked to rate on a 4-point scale (never, rarely, sometimes, often) how often each reason applied to them (Chesney et al., 2000). Other variables probed were adherence self- efficacy and beliefs about treatment effectiveness. A 4- point scale ('not sure at all' to 'very sure') was used. Two additional questions were asked: one concerned their belief in the positive effect the medicines would have on their lives and the other their view on the effects of not taking their medications precisely as directed.

Psychological distress was measured by short forms of the Center for Epidemiological Studies Depression (CES-D) scale (sum of seven four-point items, alpha coefficient = 0.85) (Mirowsky and Ross, 1992) and the Perceived Stress scale (sum of four five-point items, alpha coefficient= 0.52) (Cohen, Karmarck & Mermelstein, 1983). Patients were also asked how satisfied they were with the support from friends and family members (four-point scale, 'very dissatisfied' to 'very satisfied') and to what extent friends and family members helped them remember to take their medication (four-point scale, 'not at all' to 'a lot') (Chesney et al., 2000).

Alcohol and drug use was probed using questions on whether they had an alcoholic beverage in the last 30 days and how many drinks they usually have altogether. From these two answers an estimate of the number of alcoholic drinks consumed during the past month was made. Questions on drug usage included whether cocaine, amphetamines, heroin, and in the original questionnaire methadone treatment, had ever or in the past six months been taken (Chesney et al., 2000).

Socio-demographic questions included age, gender, ethnicity, educational status, employment status, annual income, presence of children and HIV risks.

For the purpose of this study certain changes were made to the original questionnaires:

1. The cover sheet information of the study was altered.
2. Instructions: The use of check was replaced with tick.
3. Q3. Description of oneself: this was changed since it had no relevance for South Africa.
4. Q4. Description of level of schooling completed. This was changed by dividing it into two questions reading 'what is the highest standard or grade you have passed' and ascertaining the level of post school qualifications.
5. Q6 was added to ascertain the person's home language.
6. Q7. This question was omitted. The only prominence health insurance gains in South Africa are when the medical aid actually pays for anti retroviral therapy.
7. Q8. Questions of where the person stayed were omitted.
8. Q8. Changed treatment or recovery program: South Africa would most likely not have this level of sophistication in terms of treatment. This question was omitted.
9. Option 11: No pharmacies or chemist would stock ART. This question was omitted.
10. Q19: Changed to spirits.
11. Q19b: Alteration was necessary in terms of what South Africans drink.
12. Q19c: Ounces of beer had to be translated into cans of beer.
13. Q21: The top 10 drugs used in South Africa are different to the USA: (Medical Research Council, SA).

In all other respects the schedule follows Chesney et al. (2000) and includes the following sections (see appendix 4):

A. Demographics: 1. Sex, 2. Age, 3. Racial description, 4. Level of school education, 5. Post school qualifications, 6. Home language, 7. Marital or living status, 8. Employed or not, 9. Household income since this is what is used by demographers to establish SES (Socio economic status), 10. Any Psychiatric or medical conditions, 11. Visits to doctor for HIV related treatment in the past 6 months.

B. Three questions about self-efficacy; belief in treatment and knowledge of the effects of missing doses.
C. Two questions on social support, one dealing with overall social support and another dealing with whom, if anybody, reminds the patient to take medication.
D. Fourteen questions on the possible reasons for skipping medications.
E. Daily dosages and how many tablets have to be taken each time.
F. Dosages missed within the last four days.
G. Scheduling of drugs and whether these instructions are being followed.
H. Special instructions that accompany drug taking and whether they are being followed.
I. Missing doses on weekends.
J. When last the patient missed taking a dose.
K. Center for Epidemiological Studies Depression Scale (7-point version).
L. The Perceived Stress Scale (10-point version).
M. Alcohol and Drug Usage.

Psychological Distress: The Perceived Stress scale used in the original testing by AACTG was 4-point item scale. The alpha coefficient in the original study was 0.52 (Cohen et al., 1983). In this research the 10-point scale with an alpha coefficient of 0.84 is used (Cohen et al., 1983). Since these scales were standardized on American samples the alpha coefficients for both the Center for Epidemiological Studies Depression (CES-D) scale as well as the Perceived Stress scale were calculated on data from the present sample (see page 38).

The alcohol and drug usage section: The profile of the drugs most commonly used in the Western Cape was received from a researcher at the Medical Research Council in Cape Town (Personal Communication, May 20, 2002).

3.4. Motivation for the use of self-report

For the purpose of this study the motivation for the use of self-report of adherence needs to be considered. The next section thus considers adherence measurement and why researchers have argued for the use of self- report questionnaires.

According to a number of researchers there is no "gold standard" by which adherence may be measured and it can be carried out in a number of ways (Chesney et al., 2000; Williams, 2001). Various methods have included adherence scales completed by patients, clinician assessment, pill counting, pill use and prescription, micro-processor based monitoring of drug taking, laboratory data on viral load changes, and CD4 lymphocyte counts (Friedland, 1999 in Tsasis, 2001). All of these means of assessing adherence have difficulties attached and no ideal method exists (Chesney et al., 2000; Tsasis 2001; Williams, 2001).

Self-report has been said to overestimate adherence when patients are adherent (Liu et al., 2001; Corelli, 1991 in Tsasis, 2001). However, when patients are missing doses they are likely to report this and it has been supported by detectable viral genetic material in the bloodstream (Hecht, 1998 in Chesney et al., 2000; Haubrich et al., 1999; Shelton, 1998 in Tsasis, 2001). Another study found that the self-report assessment of adherence is significantly associated with "plasma HIV concentrations" (Bangsberg, 1999, Hecht, 1998 in Chesney et al., 2000). Indirect support for structured patient report was obtained from Bangsberg et al. (2001) who found that these reports were more likely to be accurate than physician assessment when correlated with pill count. The reason according to Haubrich et al. (1999, p 1105) may be that "patients may exaggerate their adherence to please their providers." It was speculated by Bangsberg et al. (2001) that patients might be more reluctant to disclose poor adherence to their health care providers than to other interviewers and thus using self-report questionnaires would be more reliable. Further substantiation for the use of self- report was gained from Gordillo et al. (1999) who found that using a supervised pill-count and self-report gave similar adherence figures. It has also been suggested by Gordillo et al. (1999) that it is only the patients themselves who can accurately report their actual behaviour.

Kleeberger et al. (2001) states that self-reported data is a valid indicator of adherence and supports the validity of the questionnaire as a useful tool in studies. That self-reported data was a valid tool to use in studies, was also supported by Tuldra et al. (2000). Kleeberger et al. (2001) also stated that over-reporting was less likely to occur in a non- clinical setting. Self-report can be improved by limiting the length of recall that patients had to contend with and Chesney et al. (2000) suggested a period of two

days. Bangsberg et al. (2001), however, recommended that if self-report was being used people on ART should not be asked to remember beyond the last three days. Chesney et al. (2000) on the other hand, recommended that it be extended to four days so that it includes a weekend when people were less likely to follow a schedule. The focus on the most recent adherence was to maximize recall and minimize bias (Chesney et al., 2000).

Another method of assessment includes electronic monitoring which relies on a microchip in the bottle cap to record the cap being opened, but this may in effect underestimate adherence because patients tended to remove more than one dose at a time (Chesney et al., 2000; Liu et al., 2001). Electronic monitoring is an expensive way of monitoring adherence (Chesney et al., 2000). Another factor that may come into play is that patients can either throw their tablets away or even sell them (Dunbar- Jacob, 1993 in Tsasis, 2001). It was also found that pill-count tends to overestimate adherence (Liu et al., 2001).

Liu et al. (2001) suggested that at least for clinical trials, a CAS (Composite Adherence Score) was used that included MEMS (Medication Event Monitoring Scheme), a pill-count and interview. Another suggestion to check for adherence was to use the pill identification test (PIT). This test is used in conjunction with self-report and, besides supplying a back up for adherence measurement, it also improves the patient's knowledge of the treatment they are on (Parienti et al., 2000).

3.5. Data handling and statistical analysis

All data was entered onto an Excel spreadsheet. The entries were checked by having a person reading the answers from the questionnaires to another person who checked to see whether the entries were correctly entered. Any mistakes were corrected. The data was then transferred onto a Statistica spreadsheet as used at the University of Cape Town and the data analysed by using version 6.0 of this statistical package.

Data analysis was carried out in two phases. In the first phase descriptive statistics were calculated for most of the elements of the questionnaire. Further analysis consisted of performing cross tabulations and a stepwise regression analysis. This regression analysis consisted of putting in seven independent variables and submitting

it to a stepwise regression analysis with missed doses as the dependent variable or outcome variable. One of the dependent variables, substance use, had to be recoded into: 1= using a lot of alcohol or using hard or recreational drugs and 2= a little or no alcohol and marijuana use. Recoding of the outcome variable, "missing doses" (J), occurred due to the skewness of the distribution. It was recoded into three variables namely, never skipped doses, skipped dose(s) within the last month and skipped dose or doses more than three months ago. This was achieved by:

J1= J0 (never miss medication)

J2= J1 + J2 (missed more than 3 months ago + missed 1- 3 months ago)

J3= J3 + J4 + J5 (missed 2-4 weeks ago + 1-2 weeks ago + within past week).

Two scales, namely the CES- D and the Psychological distress scale were used in the questionnaire and the internal reliability was calculated for each of these scales using Cronbach's alpha. This measurement ranges from 0 (no internal reliability) to 1 (absolute internal reliability). In order to conduct the Cronbach alpha on the Perceived Stress Scale some items that were scored in a positive direction had to be recoded by using the formula: 4-score on (L4, L5, L7 and L8). Alpha scores for the two scales were 0.82 for the CES-D scale and 0.84 for the Perceived Stress scale. Because of the high alpha scores the scores in the scales were summed for each participant. Average inter item correlation for the CES-D scale was 0.42 and for the Perceived Stress scale was 0.34.

Chapter 4: Results

4.1. Introduction

Questionnaire returns from the different sites varied with some sites returning as many as 100% and others only 20%. A summary of the different sections of the questionnaire is presented, together with cross tabulations, Chi-square analysis and a Stepwise regression analysis and is followed by an overall summary of the results.

4.2. Summary of the sections

i. Background information (Section A)

Study participants consisted of 29 males and 13 females, with a mean age of 38 years (range= 27- 55). The description supplied by the participants was that 15 would describe themselves as white and 27 as black (included Black and Coloured people). The median level of education was Grade 12. More than half of the participants had some post-school qualification. Two thirds reported working for pay outside of the home. The median monthly income ranged from R2001- R5000. Twenty-four reported having a household income of less than R5000 and 17 reported having an income of more than R5000. Twenty reported English as a home language, 15 Xhosa and three Afrikaans. Twenty-four of the participants were single, 16 were either married or living with a significant other and two were either divorced, separated or widowed.

ii. Self-efficacy, treatment efficacy and knowledge of the effects of missing medication (Section B)

A vast majority (95%) believed that they could take their medication as prescribed. The belief in the efficacy of the drugs participants were given was high with 93% believing it would have a positive effect on their health. A lesser percentage (76%) believed that missing medication could make them resistant to HIV medication.

iii. Social Support (Section C)

In terms of social support 93% were satisfied with the support they received. Social support aimed at helping people to remember to take medication had a greater spread

with 45% receiving no to a little support whilst 50% receiving some to a lot of support.

iv. Complexity of regimens (Section E)

The vast majority (90%) of this sample is on bi-daily dosing. The rest are on once a day and three times a day. Complexity of the regimen could therefore not be used further as a variable because of the lack of variability in the sample. The average amount of tablets being taken for each day= 8 (std dev= 2.22). In the Chesney et al. study (2000) the participants were averaging between 10 and 25 pills per day.

v. Missed HIV medication (Section F, J and I)

Thirty eight percent of the sample (n= 16) never skips medications. The data collected indicates a high incidence of skipping doses with 26 (62%) of the participants skipping doses. Of these, 15 skipped doses more than one month ago and 11 had skipped doses within the past month. Although this figure does not indicate the frequency with which people are skipping doses it does, however, indicate that doses are being skipped and for the purposes of this study would be deemed non-adherent for the actual numbers skipping doses within the specified time frames: see histograms below. The 14% who skipped doses within two days prior to answering the questionnaire was similar to the finding of Chesney et al., (2000). Only 15%, however had skipped doses the prior weekend whereas in the Chesney et al. (2000) study, twenty one percent had skipped doses.

A large percentage of the participants had taken all their doses within the last four days. Recent non-adherence occurred: 14% had skipped doses during the prior two days. (Three (7%) had skipped doses on one day and three had skipped doses on two days). 15% had missed taking their doses during the prior weekend.

vi. Reasons for missing HIV medications (Section D)

Among participants who reported missing doses at some point in the past (N= 26), the most common reason was "feeling depressed and overwhelmed." Half reported this as one of the reasons for not taking medication. Other ranked common reasons include: a. simply forgetting, believing the drug was toxic/harmful and feeling good; b. away from home; c. busy; d. too many pills, not wanting others to notice, changes

in daily routine, felt sick, difficulty in following specified scheduling; e. avoidance of side effects, sleeping through dose and f. running out of pills. (See histograms in appendix 6).

When compared with the Kennedy (2000) study the ranking, as supplied by the South African sample, of the five top reasons why doses were skipped is very similar. On this ranking list the avoidance of side effects was low as with the Kennedy study (2000). Noticeable on this list was the number of people who believed the drugs were toxic/harmful and that feeling good meant skipping doses. A surprising result was how low down on the list "people noticing them taking medication" was.

vii. Following schedules and special instructions attached to HIV medications (Section G and H)

Eighty percent of the participants take their pills as prescribed, with approximately 10% not following instructions as to the timing of the doses.

62% of the participants have special instructions attached to taking their pills. Of these a half follow these instructions all the time, whilst another third follow the instructions most of the time to half of the time. The rest follow the instructions some of the time to never.

viii. Alcohol and Drug usage (Section M)

Nearly 60% of the participants either never use alcohol or use it only once a month. The rest are relatively evenly spread between two to three times a month to daily. Most of them do not have more than two drinks at a time, with a lesser amount having the maximum of four drinks. Only one participant used more than 12 drinks per day. In response to how many of the participants who drink, drink more than five drinks in a row (N= 24), 42% responded never, 10% drank five drinks or more in a row once a month and the rest was spread evenly between two and three times a month, once or twice a week and three to four times a week. It appears that the use of alcohol in this sample is moderate.

Participants reported very low recent use of recreational drugs (0- 10%). The drug of choice was ecstasy. Past usage included marijuana (35%), amphetamines (14%) and

cocaine/crack (14%). Of the reported percentages approximately half reported recent use. In the Chesney study 46% had used cocaine/crack and 37 % had used amphetamines.

4.3. Further analysis of data.

Further exploration of the data occurred firstly by asking the question of whether there existed a difference between friends and families assisting the black and white patients to remember to take their HIV medications (Question A3 recoded and C2). A cross-tabulation of race by social support in reminding patients to take medication was performed and submitted to a Pearson's Chi-square.

Table 1: Cross-tabulation of recoded race by support to remember medication

	Not at all	A little help	Somewhat	A lot	Total
Black	4 (23%)	2 (12%)	0	11 (65%)	17
White	12 (52%)	1 (4%)	5 (22%)	5 (22%)	23
All Grps	16	3	5	16	40

A cross-tabulation of recoded Race by Social support for remembering to take HIV medications was conducted. Pearson's Chi-square test revealed that there was a significant difference in the support offered in reminding patients to take their medication [$Chi^2 = 10.929$ (Df= 3); $p = 0.012$]. A trend was that black people seemed to receive greater support than white people in remembering to take their HIV medications. Note that with correlations all have to be treated with caution because the numbers within the different cells are small due to the small sample size and therefore only trends can be noted.

Secondly what was investigated was whether there was a difference between black and white patients in terms of adherence (Question A3 recoded and J recoded). A cross tabulation was performed and submitted to Chi-square analysis. These tests revealed that there was no difference between black and white respondents on self-reported likelihood of missing HIV medication [$Chi^2 = 2.870$ (Df= 2); $p = 0.238$].

A third question that was posed was which factors contribute to patients missing medications? This was investigated using stepwise regression. This analysis involved creating new variables namely, the outcome variable J (adherence), a single score for each individual on the CES-D scale and a single score for the Perceived stress scale and a recoded substance use (for further explanation, see methodology section).

Seven variables namely, self efficacy, belief in treatment, knowledge of the effects of skipping doses, family helping to remember medication, sum of depression scale, sum of the perceived stress scale and the recoded substance used as independent variables and whether they had skipped doses or not as the dependent variable or outcome variable.

Table 2: Stepwise regression analysis

Regression Summary for Dependent Variable: J1DV
R= .55927390 R^2= .31278729 Adjusted R^2= .27113803
F(2,33)=7.5100 p<.00205 Std.Error of estimate: .68155

		St. Err.		St. Err.		
	BETA	of BETA	B	of B	t(33)	p-level
Intercpt			2.190231	.320350	6.83699	.000000
B3	-.402584	.144625	-.318494	.114416	-2.78364	.008828
KSUM	.362463	.144625	.068270	.027240	2.50623	.017310

Although only 27 % of the variance could be explained by this regression analysis it may mean that the variance was due to other factors not tapped. The variable most likely to act as a barrier to adherence in this sample was depression (Ksum) and the variable most likely to act as a facilitator to adherence was the knowledge and belief that if medications were not taken then the participant's body could become resistant to HIV medications (B3).

4.4. Summary of results

There existed a strong belief among the participants that they could take their medication as prescribed. They also demonstrated a strong belief in the treatment they were taking. A lesser knowledge and belief was demonstrated about the effects of missing doses of drugs.

Most of the participants were satisfied with the social support they received. A strong trend emerged that blacks received more help with remembering to take their medications.

Most of the participants were on bi-daily dosing with an average of eight tablets taken per day. A large percentage had taken all their medication within the last four days before completing the questionnaire. Most took their medication on time with only 10% not following instructions. With regard to the special instructions attached to taking the medication, of the 62% with special instructions, one half followed the instructions and the rest followed the instructions most of the time to never.

The most common reasons for participants missing doses were firstly: feeling depressed and overwhelmed; secondly, equal numbers stated that they simply forgot, believed that the drugs were toxic or harmful and that they were feeling good: thirdly, that they were away from home and fourthly, that they were busy.

There was no significant difference between the races when it came to missing medications.

Alcohol and drug usage in recent months was low among these participants.

A facilitator of adherence among this sample was the knowledge and belief that if they did not take their medication their bodies would build up resistant strains of the virus. A barrier to adherence was the depression experienced by the some of the participants.

Chapter 5: Discussion and Conclusions

This chapter offers conclusions based on the results of the previous chapter. The major findings are restated and an attempt is made to place it within a South African context. Limitations of the research are discussed and suggestions for future research are made.

Patients seem to have a good knowledge of the working of the medication and a belief in the warnings against missing medication. This seems to act as a facilitator to adherence. However, what has to be noted is that the sites used are sites where clinical trials have occurred and are occurring. These patients may be trial patients and may be aware that if they do not adhere, and become resistant to the medication, their chances of being put on to another regimen may be limited. Therefore, the assumption that increasing knowledge and belief would increase adherence has certain limitations in this context. Increasing and fostering beliefs in the negative effects of not adhering may in fact be counter-productive because this kind of message holds elements of threat and fear, namely, if you do not adhere and develop resistant strains within this context then no other treatment option may be available. The scarcity of the drugs in South Africa may therefore be a facilitator in that the participants reporting of adherent behaviour may be influenced by this fact. Health promotion models should, according to Ruiter, Abraham & Kok (2000), provide specific instructions and prompts, rather than providing information that places emphasis on the negative consequences of not performing the specific behaviour.

A barrier to adherence was depression. This variable is listed in a number of studies as a factor why people do not adhere (Chesney et al., 1996; Kleeberger et al., 2001). It means that constant checking of the patient's mood is necessary and that, even if a patient does not reach a psychiatric definition of depression, counseling may be necessary. Increasing counseling with respect to depression and the lifting of this depression could affect disease progression by slowing down the process (Ikovics et al., 2000).

The sample demonstrated that they believed that they could adhere to medication regimens, believed in the medication and had a good knowledge of what missing medication would mean but cognisance needs to be taken of the discussion above. This finding means that at least for this sample it augurs well for future adherence. Having both a belief in self and a belief in treatment means that they are more likely to adhere despite side effects (Johnston Roberts, 2000).

In terms of social support a vast majority was satisfied with the support they received. A trend was that blacks received more support than whites in remembering to take medications. A parallel finding from Côte d' Ivoire was that the families of the patients involved themselves in the treatment (Dargouge, 2002). It would appear as if this is a trend that is worth investigating further.

The ranking of the five top reasons why doses were skipped in the South African sample is very similar to those supplied by patients in the Kennedy study (2000). These reasons in South Africa are: depression, forgetfulness, beliefs in toxicity and harmfulness of the drugs, feeling good and being away from home. There was an expectation that item D6, "you did not want others noticing you taking medication" could indicate a fear of being stigmatized. Patients did not rank this item highly among reasons for not adhering. When looking at this particular item, what has to be considered is that they were on twice daily dosing, and therefore if they stayed at home during these dosing times, exposure to others seeing them taking their medication became slight. An issue attached to this was: when they were away from home, were they "deliberately forgetting" to take their medication with them? This needs further investigation. On this ranking list the avoidance of side effects was low, as with the Kennedy study (2000). In South Africa it was interesting to note that not many of the participants had noted side effect profiles as the reason for not taking medication. This may also thus be attributable to the belief in self and the belief in treatment that help the patient to adhere despite side effects. In the northern hemisphere, however, Boyle (2000) stated that as more drugs had become available and AIDS had become a chronic medical condition, people were no longer wanting or willing to accept side effects.

In terms of adherence, 14% had skipped doses in the last four days. Although self-report may overestimate overall adherence, in this study the missed doses and the reason(s) for missing them were important. A concern is that if patients missed as few as five doses in a 100, then they may be at risk for the development of resistant strains of the virus (Bamberger et al., 2000b; Wainberg & Friedland, 1998). This does mean that health professionals caring for people on ART should be constantly vigilant.

The effect that the complexity of dosing regimens could have on adherence could not be carried further by this study because most of the participants were on a twice-daily dosing regimen. Orrell et al. (2001) had, however, already stated that three-times daily dosing acted as a barrier in their study. This needs to be investigated further within the South African context. These sites employed doctors who are well trained, who have been in the HIV/AIDS field for years and who were following the latest recommendations in terms of dosing. It appears therefore that if doctors were well trained and used some of the latest dosing recommendations, twice-daily dosing led to higher adherence rates than three-times daily dosing (Kemppainen et al., 2001).

A large percentage of the participants had special instructions attached to taking their medication. Of these almost three quarters followed these instructions more than half the time. The nature of the instructions or the reasons why people do not follow these instructions were not investigated within the context of this study. This needs further investigation and needs to be followed up at the sites.

The patients in this sample appear to use alcohol moderately and only a small percentage are using recreational dugs. Because of the small sample size the impact of alcohol and drugs on adherence needs to be re-investigated.

Methodological concerns within this study include sample size, language issues and questions relating to using statistical analysis on this sample size. The number of variables contained in this study needs a large sample size. A further limitation is that the sample was not random, which could lead to biases within the data. The questionnaires were only available in English and Afrikaans and no Afrikaans questionnaires were requested. Translating the questionnaire into Xhosa was not possible for this pilot study. Some participants misunderstood the instructions to

section D and filled in this section even if they had missed medications more than three months ago. A further limitation was that the length of time the participants were on the medication was not asked. This does introduce possible bias into the sample since adherence studies have found that generally adherence is high in the first few months but declined over a year (Tuldra et al., 2000). A limitation also of this study was that self-reported adherence was used. Self-report, although having its advantages also have disadvantages such as patients overestimating adherence. Therefore this study could have had a clinical perspective attached such as a viral load count.

For a study such as this it would have been preferable to have a research assistant at the site to deal with any queries. Errors were possible because if the respondent had difficulties, they often had to ask the nurse in charge for help. Biases therefore are a distinct possibility in answering questions relating to adherence to medication.

The sample size dictated the amount of statistics and the type of statistics that could be performed. This also leads to care being taken with making predictions to a wider population. No significant correlation was found between race and adherence. Although a significant correlation was found between race and social support, such as that people were helping subjects to remember to take their medication, the only conclusion that can be drawn from a sample of this size is that it indicates a trend that needs further investigation.

The sample size dictated that, in order to do a stepwise regression, seven variables had to be chosen. These variables were checked against the weighting of the various factors in the literature. In the stepwise regression analysis two of the variables, notably KSum (CES-D) and LSum (Perceived Stress Scale) were highly positively correlated. This introduced multi-colinearity into the regression analysis and a decision had to be made to use one or the other. KSum was used because of its higher zero order correlation (KSum corr.= O.35 with dependent variable and LSum corr.= 0.22 with dependent variable).

Using a stepwise regression with small sample size has certain limitations. The purpose with a regression analysis is the construction of a model, but because the cells

have such small numbers, the model cannot be used for predictive purposes. Another difficulty was that the sample was not random. A possible way to test this model would have been to collect a new sample and to run the regression. At this point, because a new sample was not available, no cross validation is possible. Also within this regression model it has to be noted that for example, social support and depression may be interconnected but because depression is a stronger variable in this regression, social support is excluded from the regression.

Despite these limitations, this study adds to the literature on adherence issues within a developing country. A facilitator to adherence was the belief and knowledge surrounding the consequences of not adhering to antiretroviral medication. Using patients on drug trials within a developing country adds dynamics to findings that needs further investigation. Additional research within this context is indicated in how much fear/ threat is optimal for adherence. The exact nature of the factors that are contributing to the depression felt by HIV positive people on ART in this sample needs to be investigated. A further investigation could be the prevalence of depressive symptoms in PLWHA on ART in South Africa. A significant trend within this sample was that black families were involved in assisting patients with medication adherence. This trend needs further investigation. Although stigmatization with regard to adherence to medication appeared not to be an issue among this sample, this may have been because of the regimen requirements. It has, however, been shown that stigma is a barrier to adherence in TB medication (Dick, 1998). It may therefore be possible that if people on ART had to take medication in public or the workplace, they may feel the effects of stigmatization. However, this needs to be investigated further. Further research is also needed to investigate what the difficulties are in following the specific instructions attached to taking ART as well as finding ways of improving the numbers of people following these specific instructions.

The access to ART in the public health system is an increasing possibility. However, in order to utilize resources optimally, continuing research needs to be done in order to identify facilitators and barriers so that facilitators can be promoted and barriers can be minimized.

Because research on adherence is limited in South Africa, pilot studies such as this are important. The scarcity of the relevant drugs in South Africa means that the numbers of participants available for study are limited and trials sites have to be used, as with this study. This does, however, complicate the analyses of the data gained within this context. This suggests that much more research is needed to develop adherence models that are appropriate to a developing country context, and that an important investment the government needs to make is supporting research of this nature.

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Appendix 1: Cover letter to participants

Dear Participant

My name is Graeme Hendricks and I am a Master's student in clinical psychology at the University of Cape Town. My interest in adherence to anti- retroviral medication comes from my long involvement in the fight against HIV/AIDS and the care of People Living with HIV/AIDS.

This research forms part of my course work for my degree. However I will find some way to put the insights you share with me into practice. I will not only by sharing the findings with colleagues but also with students. I will not however be revealing the sites of the research. A publication is a possibility.

Thanking you in anticipation of a completed questionnaire.

Yours sincerely

Graeme Hendricks

Appendix 2: ACTG Baseline adherence questionnaire II

Source: http://www.fstrf.org/qol/adult_ql.html

Date of retrieval: 20 April 2002.

ACTG BASELINE ADHERENCE QUESTIONNAIRE II

NIAID ADULT AIDS CLINICAL TRIALS GROUP

Patient Number | | | | | | | | Date of Patient Visit | | | | | | | | mmm dd yy

Protocol Number | 0 | 0 | 0 | | | | Institution Code | | | | | | |

Form Week | 0 | 0 | 0 | Key Operator Code | | | |

FOR OFFICE USE ONLY - TEAR OFF SHEET

INSTRUCTIONS TO THE STUDY NURSE:

The BASELINE ADHERENCE QUESTIONNAIRE II SHOULD BE GIVEN TO THE SUBJECT PRIOR TO THE CLINICAL EXAM. The subject must be able to read at the sixth-grade level at a minimum to complete the questionnaire without additional assistance.

It is important to be familiar with the content and format of the questionnaire before giving it to study participants. At the first visit, please begin by telling the participant:

- The purpose of this form is to learn about potential influences of treatment adherence.
- Please answer all questions honestly; you will not be "judged" based on your responses.
- If you do not wish to answer a question, please draw a line through it.
- When completed, the form will be quickly reviewed to make sure you didn't mistakenly skip questions (without crossing them out); your specific responses to questions will not be reviewed.
- Please feel free to ask if you need any of the questions explained to you.

You should then briefly go over the format of the questions and how to complete them. The questionnaire is very brief and should take no more than 10 minutes to complete. Before giving the subject the questionnaire, please fill out the header(s) and DETACH THIS PAGE.

Each question is in the same general format and contains several items. Note that the subject is always asked to make a "✓" next to the appropriate category.

Collect the completed questionnaire before the clinical exam. Before going on, review the questionnaire for omissions. If the participant missed any of the questions, point this out and encourage him/her to complete the omissions.

For data keying, if the subject did not answer a question, enter "-1." Do not leave any fields blank.

PLEASE COMPLETE THE FOLLOWING ITEMS AFTER SUBJECT COMPLETES THE QUESTIONNAIRE OR AFTER YOU ASCERTAIN THAT THIS IS NOT POSSIBLE:

1. How was the questionnaire completed? ..... 1-Self administered by the study participant
   2-Face-to-face interview that you conducted
   3-Both self-administered and interview
   4-Not completed
   9-Other, specify

   If Other, specify [30]: _____

   a. If you answered "4-Not completed," please indicate the reason why :
      1-Subject refused
      2-Subject missed clinic visit
      3-There was not enough time
      9-Other reason, specify

   If Other, specify [30]: _____

ACTG BASELINE ADHERENCE QUESTIONNAIRE II

NIAID ADULT AIDS CLINICAL TRIALS GROUP

Patient Number | Date of Patient Visit (mmm dd yy)

Protocol Number 0 0 0 | Institution Code

Form Week 0 0 0 | Key Operator Code

The answers you give on this form will be used to plan ways to help other people who must take pills on a difficult schedule. Please do the best you can to answer all the questions. If you do not wish to answer a question, please draw a line through it. If you do not know how to answer a question, ask your study nurse to help. Thank you for helping in this important study.

INSTRUCTIONS: Please answer the following questions by placing a "✓" in the appropriate box.

A. How sure are you that:

Please check one box for each question. ***(Check one)***

	Not At All Sure	Somewhat Sure	Very Sure	Extremely Sure
1. You will be able to take all or most of the study medication as directed?	☐ 0	☐ 1	☐ 2	☐ 3
2. The medication will have a positive effect on your health?	☐ 0	☐ 1	☐ 2	☐ 3
3. If you do not take this study medication exactly as instructed, the HIV in your body will become resistant to HIV medications?	☐ 0	☐ 1	☐ 2	☐ 3

B. The following questions ask about your social support.

Please check one box for each question. ***(Check one)***

	Very Dissatisfied	Somewhat Dissatisfied	Somewhat Satisfied	Very Satisfied
1. In general, how satisfied are you with the overall support you get from your friends and family members?	☐ 0	☐ 1	☐ 2	☐ 3

	Not At All	A Little	Somewhat	A lot	Not Applicable
2. To what extent do your friends or family members help you remember to take your medication?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

Patient Number ☐☐☐☐☐☐☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐ (mmm dd yy)

C. People may miss taking their medications for various reasons. Here is a list of possible reasons why you may have missed taking any medications within the **past month.**

If you have **NOT** taken **any** medications within the **past month**, please check this box and skip to Section D: ..... ☐ 1

In the **past month**, how often have you **missed taking your medications** because you:

(Check one)

Please check one box for each question.	**Never**	**Rarely**	**Some-Times**	**Often**
1. Were away from home?	☐ 0	☐ 1	☐ 2	☐ 3
2. Were busy with other things?	☐ 0	☐ 1	☐ 2	☐ 3
3. Simply forgot?	☐ 0	☐ 1	☐ 2	☐ 3
4. Had too many pills to take?	☐ 0	☐ 1	☐ 2	☐ 3
5. Wanted to avoid side effects?	☐ 0	☐ 1	☐ 2	☐ 3
6. Did not want others to notice you taking medication?	☐ 0	☐ 1	☐ 2	☐ 3
7. Had a change in daily routine?	☐ 0	☐ 1	☐ 2	☐ 3
8. Felt like the drug was toxic/harmful?	☐ 0	☐ 1	☐ 2	☐ 3
9. Fell asleep/slept through dose time?	☐ 0	☐ 1	☐ 2	☐ 3
10. Felt sick or ill?	☐ 0	☐ 1	☐ 2	☐ 3
11. Felt depressed/overwhelmed?	☐ 0	☐ 1	☐ 2	☐ 3
12. Had problem taking pills at specified times (with meals, on empty stomach, etc.)?	☐ 0	☐ 1	☐ 2	☐ 3
13. Ran out of pills?	☐ 0	☐ 1	☐ 2	☐ 3
14. Felt good?	☐ 0	☐ 1	☐ 2	☐ 3

D. When was the last time you missed taking any of your medications?

(Check one box)

Within the past week	5 ☐
1-2 weeks ago	4 ☐
2-4 weeks ago	3 ☐
1-3 months ago	2 ☐
More than 3 months ago	1 ☐
Never skip medications or not applicable	0 ☐

ACTG BASELINE ADHERENCE QUESTIONNAIRE II

Patient Number ☐☐ ☐☐☐☐ ☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐ (mmm dd yy)

E. In the **past week** how often did you:

Please check one box for each question.

	Never/ Rarely	Sometimes	Often	Mostly or Always
	(Check one)			
1. Feel like you couldn't shake off the blues even with help from your family or friends?	☐ 0	☐ 1	☐ 2	☐ 3
2. Have trouble keeping your mind on what you were doing?	☐ 0	☐ 1	☐ 2	☐ 3
3. Feel that everything you did was an effort?	☐ 0	☐ 1	☐ 2	☐ 3
4. Have trouble sleeping?	☐ 0	☐ 1	☐ 2	☐ 3
5. Feel lonely?	☐ 0	☐ 1	☐ 2	☐ 3
6. Feel sad?	☐ 0	☐ 1	☐ 2	☐ 3
7. Feel like you just couldn't "get going"?	☐ 0	☐ 1	☐ 2	☐ 3

F. In the **past month**, how often have you:

Please check one box for each question.

	Never	Almost Never	Some-times	Fairly Often	Very Often
			(Check one)		
1. Been upset because of something that happened unexpectedly?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2. Felt unable to control the important things in your life?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
3. Felt nervous and "stressed"?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
4. Felt confident in your ability to handle your personal problems?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
5. Felt that things were going your way?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
6. Found that you could not cope with all the things that you had to do?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
7. Been able to control irritations in your life?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
8. Felt that you were on top of things?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
9. Been angered because of things that happened that were outside of your control?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
10. Felt problems were piling up so high that you could not overcome them?	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

Patient Number ☐☐☐☐☐☐☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐ (mmm dd yy)

G. People have various health habits. The following questions ask about your alcohol and drug use, past and current.

1. How often have you had a drink containing alcohol - a glass of beer, wine, a mixed drink, or any kind of alcoholic beverage - in the last 30 days? ***(Check one)***

Daily	Nearly Every Day	3 or 4 Times A Week	Once or Twice A Week	2 or 3 Times A Month	Once A Month	Never
☐ 6	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0

If Never, skip ahead to question 4.

2. On days when you drank any alcoholic beverages, in the last 30 days, how many drinks did you usually have altogether? By a drink, we mean a can or glass of beer, a 4-ounce glass of wine, a 1½ ounce shot of liquor, or a mixed drink with 1½ ounces of liquor. ***(Check one)***

1 or 2 Drinks Per Day	3 or 4 Drinks Per Day	5 or 6 Drinks Per Day	7 or 8 Drinks Per Day	9 - 11 Drinks Per Day	12 or More Drinks Per Day
☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. During the past 30 days, how often have you had 5 or more drinks of alcohol in a row, that is, within a couple of hours (e.g., 2-4 hours)? ***(Check one)***

Daily	Nearly Every Day	3 or 4 Times A Week	Once or Twice A Week	2 or 3 Times A Month	Once A Month	Never
☐ 6	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1	☐ 0

4. Please check "Yes" or "No" for each question:

a. ☐ Yes (1) ☐ No (2) Have you ever used marijuana?
If you used this drug, have you used it within the past 6 months? ☐ Yes (1) ☐ No (2)

b. ☐ Yes (1) ☐ No (2) Have you ever used cocaine (powder, crack, freebase)?
If you used this drug, have you used it within the past 6 months? ☐ Yes (1) ☐ No (2)

c. ☐ Yes (1) ☐ No (2) Have you ever used heroin?
If you used this drug, have you used it within the past 6 months? ☐ Yes (1) ☐ No (2)

d. ☐ Yes (1) ☐ No (2) Have you ever used amphetamines (speed)?
If you used this drug, have you used it within the past 6 months? ☐ Yes (1) ☐ No (2)

Patient Number ☐☐☐☐☐☐☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐
mmm dd yy

5. Are you **currently** in methadone treatment? ..... ☐ Yes 1 ☐ No 2
   If Yes, skip to Question H.
   If No, have you **ever** been in methadone treatment? ..... ☐ Yes 1 ☐ No 2

H. These last questions ask about your background.

1. What is the highest level of education you have completed? ***(Check one box)***

11th grade or less	0 ☐
High school graduate or GED	1 ☐
2 years of college/AA degree/Technical school training	2 ☐
College graduate (BA or BS)	3 ☐
Master's degree	4 ☐
Doctorate/medical degree/law degree	5 ☐

2. What is (are) the most likely way(s) that you became infected with HIV?
   (Check "Yes" or "No" for each question.)

	Yes	No
a. Sex with a man who was HIV+	1☐	2☐
b. Sex with a woman who was HIV+	1☐	2☐
c. Shared needles with a person who was HIV+	1☐	2☐
d. Blood transfusion or other medical procedure	1☐	2☐
e. Don't know	1☐	2☐
f. Other (needle stick at work, etc.)	1☐	2☐

   If Other, please specify: _____

3. Do you work for pay outside the home? ☐ Yes 1 ☐ No 2

4. Do you have any children? ☐ Yes 1 ☐ No 2
   If Yes, how many live with you? ..... ☐☐

Thank you very much for completing these questions.
The information that you provided will help with the development of better drug regimens for all subjects with HIV.

Language: English **E**

Date Form Keyed (DO NOT KEY): _____/_____/_____

Appendix 3: ACTG Adherence follow-up questionnaire

Source: http://www.fstrf.org/qol/adult_ql.html

Date of retrieval: 20 April 2002.

ACTG ADHERENCE FOLLOW-UP QUESTIONNAIRE

NIAID ADULT AIDS CLINICAL TRIALS GROUP

Patient Number ☐☐☐☐☐☐☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐ (mmm dd yy)

Protocol Number 0 0 0 ☐☐☐ Institution Code ☐☐☐☐☐☐

Form Week ☐☐☐ Key Operator Code ☐☐☐

FOR OFFICE USE ONLY - TEAR OFF SHEET

INSTRUCTIONS TO THE STUDY PERSONNEL:

The ACTG ADHERENCE FOLLOW-UP QUESTIONNAIRE SHOULD BE GIVEN TO THE SUBJECT PRIOR TO THE CLINICAL EXAM. The subject must be able to read at the sixth-grade level at a minimum to complete the questionnaire without additional assistance.

It is important to be familiar with the content and format of the questionnaire before giving it to study participants. At the first visit, please begin by telling the participant:

- The purpose of this form is to learn about potential influences of treatment adherence.
- Please answer all questions honestly; you will not be "judged" based on your responses.
- If you do not wish to answer a question, please draw a line through it.
- When completed, the form will be quickly reviewed to make sure you didn't mistakenly skip questions (without crossing them out); your specific responses to questions will not be reviewed.
- Please feel free to ask if you need any of the questions explained to you.

For question "A," review with the subject what treatment they are receiving and complete the worksheet together. You should then briefly go over the format of the questions and how to complete them.

The questionnaire is very brief and should take no more than 5 minutes to complete. Before giving the subject the questionnaire, please fill out the header(s) and DETACH THIS PAGE.

Each question is in the same general format and contains several items. Note that the subject is always asked to make a "✓" next to the appropriate category. Drug names and abbreviations of the most common anti-HIV drugs and of any other study drugs have been included on the worksheet for reference and use.

Collect the completed questionnaire before the clinical exam. Before going on, review the questionnaire for omissions. If the participant missed any of the questions, point this out and encourage him/her to complete the omissions.

For data keying, if the subject did not answer a question, enter "-1." Do not leave any fields blank.

PLEASE COMPLETE THE FOLLOWING ITEMS AFTER SUBJECT COMPLETES THE QUESTIONNAIRE OR AFTER YOU ASCERTAIN THAT THIS IS NOT POSSIBLE:

1. How was the questionnaire completed? .... ☐
   1-Self administered by the study participant
   2-Face-to-face interview that you conducted
   3-Both self-administered and interview
   4-Not completed
   9-Other, specify

   If Other, specify [30]: ____________________

   a. If you answered "4-Not completed," please indicate the reason why : ☐
      1-Subject refused
      2-Subject missed clinic visit
      3-There was not enough time
      9-Other reason, specify

   If Other, specify [30]: ____________________

ACTG ADHERENCE FOLLOW-UP QUESTIONNAIRE

Patient Number | Date of Patient Visit (mmm dd yy)

Protocol Number 0 0 0 | Institution Code

Form Week | Key Operator Code

THIS PAGE IS TO BE COMPLETED BY THE SUBJECT AND STUDY PERSONNEL TOGETHER.

INSTRUCTIONS: Complete this worksheet with the subject. Drug names and abbreviations of the possible study medications have been included for your reference and use. Use the abbreviations indicated (i.e., "APV" for Amprenavir).

A. You are currently taking the following study drugs at the frequency and doses listed:

Study Regimen		
Study Drug Abbreviation/Name and Dose	**# Pills Each Time (Pills Each Dose)**	**# Times Per Day (Doses Per Day)**

Anti-HIV Drugs	
Abacavir/ABC/Ziagen/1592U89	GW433908
Alovudine/CL-184824	Indinavir/IDV/Crixivan
Amprenavir/APV/Agenerase/141W94/VX-479	Interleukin-2/IL-2
Atazanavir/ATV/BMS-232632	Lamivudine/3TC/Epivir
Atevirdine mesylate U-87201E	Lopinavir/Ritonavir (LPV/RTV)/Kaletra ABT-378/r
Azidouridine/AzdU/azido-2',3'-dideoxyuridine	Loviride/Lotrene
AZT/ZDV/Zidovudine/Retrovir	Nelfinavir/NFV/Viracept
CD4/RST4	Nevirapine/NVP/Viramune
Combivir (3TC/ZDV)	Ritonavir/RTV/Norvir
d4T/Stavudine/Zerit	Saquinavir soft gel/FTV/Fortovase
ddC/Zalcitabine/HIVID	Saquinavir (HGC)/SQV/Invirase/R031-8959
ddI/Didanosine/Videx	T-20/pentafuside
DLV/delavirdine mesylate/Rescriptor	TDF/Tenofovir/Tenofovir disoproxil fumarate/Viread
Efavirenz/EFV/Sustiva/DMP266	Trizivir (3TC/ABC/ZDV)
Fluorouridine/935U83	
FTC/coviracil/emtricitabine	

Patient Number ☐☐ ☐☐☐☐☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐
mmm dd yy

The answers you give on this form will be used to plan ways to help other people who must take pills on a difficult schedule. Please do the best you can to answer all the questions. If you do not wish to answer a question, please draw a line through it. If you do not know how to answer a question, ask your study nurse to help. Thank you for helping in this important study.

SUBJECT ONLY continue here.

The next section of the questionnaire asks about your study medications that you took over the last four days. Drug codes and abbreviations of the possible study medications have been included for your reference and use on page 2.

☞ Most people with HIV have many pills to take at different times during the day. Many people find it hard to always remember their pills:

- Some people get busy and forget to carry their pills with them.
- Some people find it hard to take their pills according to all the instructions, such as "with meals" or "on an empty stomach," "every 8 hours," "with plenty of fluids."
- Some people decide to skip pills to avoid side effects or to just not be taking pills that day.

We need to understand how people with HIV are really doing with their pills. Please tell us what you are **actually** doing. Don't worry about telling us that you don't take all your pills. We need to know what is really happening, not what you think we "want to hear."

1. The next section of the questionnaire asks about the study medications that you may have **missed** taking over the last four days. Please complete the table below, using one line for each study medication you are taking, and using the abbreviations on the previous page. If you did not miss any doses, write a zero (0) in the box. Note that the table asks about DOSES, not PILLS.

   IF YOU TOOK ONLY A PORTION OF A DOSE ON ONE OR MORE OF THESE DAYS, PLEASE REPORT THE DOSE(S) AS BEING MISSED.

Step 1	HOW MANY DOSES DID YOU MISS...			
	Step 2	Step 3	Step 4	Step 5
Abbreviations/Names of your study drugs	Yesterday	Day before yesterday (2 days ago)	3 days ago	4 days ago
	☐ doses	☐ doses	☐ doses	☐ doses
	☐ doses	☐ doses	☐ doses	☐ doses
	☐ doses	☐ doses	☐ doses	☐ doses
	☐ doses	☐ doses	☐ doses	☐ doses
	☐ doses	☐ doses	☐ doses	☐ doses
	☐ doses	☐ doses	☐ doses	☐ doses
	☐ doses	☐ doses	☐ doses	☐ doses

ACTG ADHERENCE FOLLOW-UP QUESTIONNAIRE

Patient Number ☐☐ ☐☐☐☐ ☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐
mmm dd yy

The following questions pertain to the study regimen on page 2.

If you took only a <u>portion</u> of a dose on one or more of these days, please report the dose(s) as being <u>missed.</u>

B. During the past 4 days, on **how many days** have you missed taking **all your doses?**

(Check one box)

None	0 ☐
One day	1 ☐
Two days	2 ☐
Three days	3 ☐
Four days	4 ☐

C. Most study medications need to be taken on a schedule, such as "2 times a day" or "3 times a day" or "every 8 hours." How closely did you follow your specific schedule over the last four days?

Never	Some Of The Time	About Half Of The Time	Most Of The Time	All Of The Time
☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

D. Do any of your study medications have special instructions, such as "take with food" or "on an empty stomach" or "with plenty of fluids"?

☐ **Yes** 1 ☐ **No** 2

If Yes, how often did you follow those special instructions over the last **four** days?

Never	Some Of The Time	About Half Of The Time	Most Of The Time	All Of The Time
☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

E. Some people find that they forget to take their pills on the weekend days. Did you miss any of your study medications last weekend - last Saturday **or** Sunday?

☐ **Yes** 1 ☐ **No** 2

F. When was the last time you missed any of your medications?

(Check one box)

Within the past week	5 ☐
1-2 weeks ago	4 ☐
2-4 weeks ago	3 ☐
1-3 months ago	2 ☐
More than 3 months ago	1 ☐
Never skip medications	0 ☐

*If you **Never** miss your study medications, please STOP.*
Otherwise, please continue by answering the next set of questions.

ACTG ADHERENCE FOLLOW-UP QUESTIONNAIRE

Patient Number ☐☐ ☐☐☐☐ ☐ Date of Patient Visit ☐☐☐ ☐☐ ☐☐ (mmm dd yy)

G. People may miss taking their study medications for various reasons. Here is a list of possible reasons why you may miss taking your medications. How often have you **missed taking your study medications** because you: ***(Check one)***

Please check one box for each question.	**Never**	**Rarely**	**Sometimes**	**Often**
1. Were away from home?	☐ 0	☐ 1	☐ 2	☐ 3
2. Were busy with other things?	☐ 0	☐ 1	☐ 2	☐ 3
3. Simply forgot?	☐ 0	☐ 1	☐ 2	☐ 3
4. Had too many pills to take?	☐ 0	☐ 1	☐ 2	☐ 3
5. Wanted to avoid side effects?	☐ 0	☐ 1	☐ 2	☐ 3
6. Did not want others to notice you taking medication?	☐ 0	☐ 1	☐ 2	☐ 3
7. Had a change in daily routine?	☐ 0	☐ 1	☐ 2	☐ 3
8. Felt like the drug was toxic/harmful?	☐ 0	☐ 1	☐ 2	☐ 3
9. Fell asleep/slept through dose time?	☐ 0	☐ 1	☐ 2	☐ 3
10. Felt sick or ill?	☐ 0	☐ 1	☐ 2	☐ 3
11. Felt depressed/overwhelmed?	☐ 0	☐ 1	☐ 2	☐ 3
12. Had problem taking pills at specified times (with meals, on empty stomach, etc.)?	☐ 0	☐ 1	☐ 2	☐ 3
13. Ran out of pills?	☐ 0	☐ 1	☐ 2	☐ 3
14. Felt good?	☐ 0	☐ 1	☐ 2	☐ 3

Thank you very much for completing these questions.

The information that you provided will help with the development of better drug regimens for all subjects with HIV.

Language: English ☐ **E**

Date Form Keyed (DO NOT KEY): _____ / _____ / _____

Appendix 4: Questionnaire used in the present study (English and Afrikaans versions).

Many people taking HIV medications sometimes find it difficult to remember what pills to take, when to take them, how to take them (with food - without food) and for other reasons.

By assisting us with this questionnaire you will be helping us to research these difficulties and help find possible solutions to overcome them. We need you to be open and honest about how you feel in having to take these medications daily, and possibly for life.

It is voluntary to answer these questions and the answers you give us will not be shared with your relatives or friends. All answers will be confidential.

Do <u>not</u> write your name.

Thank You Very Much For Your Help.

Instructions: Please read each question carefully. Tick "√ " the answer of your choice or answer in writing.
There is no right or wrong answer.

A: Background Information:

1. What is your sex?

Male	1
Female	2

2. How old are you?

3. How would you describe yourself?

Black	1
White	2
Coloured	3
Indian / Asian	4
Other	5

If "Other", please specify _____

4. What is the highest standard or grade you have passed?

_____

5. Do you have any post-school qualifications?

Yes	1
No	2

If "YES" - please specify _____

6. What is your home language?

English	1
Xhosa	2
Afrikaans	3
Other	4

If "Other", please specify _____

7. Are you?

Single	1
Married or Living with significant other	2
Separated; Divorced; Widowed	3

8. Do you work for pay outside the home?

Yes	1
No	2

9. What is your household income?

R0- R500	1
R501- R1000	2
R1001- R2000	3
R2001- R5000	4
R5001- R8000	5
R8001- R10000	6
More than R10000	7

10. Do you currently take prescribed pills for any of the following?

	Yes	No
1. Psychiatric problem (e.g. for your nerves)	1	2
2. High blood pressure	1	2
3. Sugar	1	2
4. Arthritis/rheumatism	1	2
5. Tuberculosis/TB	1	2
6. Cancer	1	2
7. Other (Specify _____)	1	2

11. Have you visited your doctor in relation to treatment for HIV/AIDS in the past six months

Yes	1
No	2

If YES - How many times did you visit your doctor?

1 - 2 times	1
3 - 4 times	2
More than 4 times	3

Instructions: Please answer the following questions by placing an "√ " in the appropriate box.

B: The questions below are about taking medications for HIV/AIDS.

Please tick one box for each question: (Tick one)

	Not At All Sure	Somewhat Sure	Very Sure	Extremely Sure
1. How sure are you that you will be able to take all or most of the HIV medication as directed?	0	1	2	3
2. How sure are you that the HIV medication will have a positive effect on your health?	0	1	2	3
3. How sure are you that if you do not take the HIV medication exactly as instructed, the HIV in your body will become resistant to HIV medications?	0	1	2	3

C: The following questions ask about your social support.

Please tick one box for each question: (Tick one)

	Very Dissatisfied	Somewhat Dissatisfied	Somewhat Satisfied	Very Satisfied
1. In general, how satisfied are you with the overall support you get from your friends and family members?	0	1	2	3

	Not At All	A Little	Somewhat	A Lot	Not Applicable
2. To what extent do your friends or family members help you remember to take your medications?	0	1	2	3	4

D: People may miss taking their HIV medication for various reasons. Here is a list of possible reasons why you may have missed taking any medication within the past month.

In the past month, how often have you missed taking your HIV medication/pills because:
Please tick one box for each question: (Tick one)

	Never	Rarely	Sometimes	Often
1. You were away from home?	0	1	2	3
2. You were busy with other things?	0	1	2	3
3. You simply forgot?	0	1	2	3
4. You had too many pills/tablets to take?	0	1	2	3
5. You wanted to avoid side effects?	0	1	2	3
6. You did not want others to notice you taking medication?	0	1	2	3
7. You had a change in daily routine?	0	1	2	3
8. You felt like the drug was toxic/harmful?	0	1	2	3
9. You fell asleep/slept through the dose time?	0	1	2	3
10. You felt sick or ill?	0	1	2	3
11. You felt depressed/overwhelmed?	0	1	2	3
12. You had problems taking the pills/tablets at specified times (with meals, on empty stomach, etc)?	0	1	2	3
13. You ran out of pills/tablets?	0	1	2	3
14. You felt good?	0	1	2	3

Instructions: Please answer the following questions by placing an "✓ " in the appropriate box.

E: The next section asks how many and how often you take medication for HIV/AIDS.

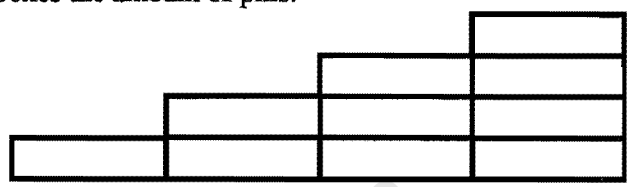
1. I have to take my pills: (tick one box)

Once a day	1
Twice a day	2
Three times a day	3
Four times a day	4

2. How many pills do you take for each dose?

Please write in the appropriate box/boxes the amount of pills.

Once a day
Twice a day
Three times a day
Four times a day



F: The next section asks about the HIV medication that you may have missed taking over the past four days.

If you only took a portion of a dose on one or more of these days, please report the dose(s) as being missed.

1. During the past four days, on how many days have you missed taking all your doses?

(tick one box)

None	0
One day	1
Two days	2
Three days	3
Four days	4

G: Most HIV medications need to be taken on a schedule, such as "twice a day" or "three times a day" or "every 8 hours".

1. How closely did you follow your instructions to take your HIV pills? (tick one box)

Never	0
Some of the time	1
About half of the time	2
Most of the time	3
All of the time	4

H: Do any of your HIV medications have special instructions, such as "take with food" or "on an empty stomach" or "with plenty fluids"?

(tick one box)

Yes	0
No	1

If YES - How often did you follow those special instructions over the past four days?

(tick one box)

Never	0
Some of the time	1
About half of the time	2
Most of the time	3
All of the time	4

I: Some people find that they forget to take their HIV pills on the weekend days. Did you miss any of your medications last weekend (last Saturday or Sunday)?

(tick one box)

Yes	0
No	1

J: When was the last time you missed taking any of your HIV medications?

(tick one box)

Within the past week	5
1 - 2 weeks ago	4
2 - 4 weeks ago	3
1 - 3 months ago	2
More than three months ago	1
I never skip medications	0

K: The next section asks how you have been feeling.

Please tick one box for each question: (Tick one)

	Never/ Rarely	Sometimes	Often	Mostly or Always
1. In the past week, how often did you feel like you couldn't shake off the blues even with the help from your family or friends?	0	1	2	3
2. In the past week, how often did you have trouble keeping your mind on what you were doing?	0	1	2	3
3. In the past week, how often did you feel that everything you did was an effort?	0	1	2	3
4. In the past week, how often did you have trouble sleeping?	0	1	2	3
5. In the past week, how often did you feel lonely	0	1	2	3
6. In the past week, how often did you feel sad?	0	1	2	3
7. In the past week, how often did you feel like you just couldn't "get going"?	0	1	2	3

L. In the past month, how often have you:

Please tick one box for each question: (Tick one)

	Never	Almost Never	Some-times	Fairly Often	Very Often
1. Been upset because of some-thing that happened unexpectedly?	0	1	2	3	4
2. Felt unable to control the important things in your life?	0	1	2	3	4
3. Felt nervous and "stressed"?	0	1	2	3	4

L. (Continued) In the past month, how often have you:

Please tick one box for each question: (Tick one)

	Never	Almost Never	Some-times	Fairly Often	Very Often
4. Felt confident in your ability to handle your personal problems?	0	1	2	3	4
5. Felt that things were going your way?	0	1	2	3	4
6. Found that you could not cope with all the things that you had to do?	0	1	2	3	4
7. Been able to control irritations in your life?	0	1	2	3	4
8. Felt that you were on top of things?	0	1	2	3	4
9. Been angered because of things that happened that were outside of your control?	0	1	2	3	4
10. Felt that problems were piling up so high that you could not overcome them?	0	1	2	3	4

M: People have various health habits. The following questions ask about your alcohol and drug use, past and current.

1. How often have you had a drink containing alcohol - a glass of beer, wine, a mixed drink, or any kind of alcoholic beverage - in the past 30 days?

(tick one box)

Daily	6
Nearly every day	5
3 or 4 times a week	4
Once or twice a week	3
2 or 3 times a month	2
Once a month	1
Never	0

If NEVER - Skip to question 4.

2. On days when you drank alcoholic beverages, in the past 30 days, how many drinks did you usually have altogether? By a drink, we mean a can or glass of beer, a glass of wine, a tot of spirits/liquor, or a mixed drink with a tot of spirits/liquor.

(tick one box)

1 or 2 drinks per day	0
3 or 4 drinks per day	1
5 or 6 drinks per day	2
7 or 8 drinks per day	3
9 - 11 drinks per day	4
12 or more drinks per day	5

3. During the past 30 days, how often have you had 5 or more drinks of alcohol in a row, that is, within a couple of hours (e.g., 2-4 hours)?

(tick one box)

Daily	6
Nearly every day	5
3 or 4 times a week	4
Once or twice a week	3
2 or 3 times a month	2
Once a month	1
Never	0

4. Please tick "YES" or "NO" for each question:

a: Have you ever used marijuana/ dagga?

Yes	1
No	2

If YES - Have you used it within the past six months?

Yes	1
No	2

b: Have you ever used mandrax/ buttons?

Yes	1
No	2

If YES - Have you used it within the past six months?

Yes	1
No	2

c: Have you ever used heroin?

Yes 1
No 2

If YES - Have you used it within the past six months?

Yes 1
No 2

d: Have you ever used amphetamines (speed)?

Yes 1
No 2

If YES - Have you used it within the past six months?

Yes 1
No 2

e: Have you ever used cocaine (coke/ crack/ freebase)?

Yes 1
No 2

If YES - Have you used it within the past six months?

Yes 1
No 2

f: Have you ever used ecstasy ("e")?

Yes 1
No 2

If YES - Have you used it within the past six months?

Yes 1
No 2

Thanks for taking the time to answer these questions. We appreciate your efforts and contributions.

Baie mense wat MIV medikasie moet neem, vind dit soms moeilik om te onthou watter pille om te neem, wanneer om die pille te neem, hoe om die pille te neem (met maaltye, nie met maaltye) en om 'n verskeidendheid ander redes.

Met jou samewerking deur die vraelys te beantwoord, sal jy ons help om hierdie redes na te vors en om met moontlike oplossings vorendag te kom. Wees asseblief oop en eerlik oor jou gevoelens omdat jy hierdie medikasie daagliks en moontlik vir altyd moet neem.

Die beantwoording van die vraelys is vrywillig. Jou antwoorde is vertroulik en sal nie met jou vriende of familie gedeel word nie.

Moenie jou naam op die vraelys neerskryf nie.

Baie danke vir jou samewerking.

Instruksies: Lees asseblief elke vraag aandagtig deur. Merk " /" die antwoord van jou keuse, of skryf die antwoord neer. Daar is geen regte of verkeerde antwoorde nie.

A: Agtergrond:

1. Wat is jou geslag?

Manlik	1
Vroulik	2

2. Hoe oud is jy?

3. Hoe beskryf jy jouself?

Swart	1
Wit	2
Kleurling	3
Indiër/Asiaties	4
Ander	5

Indien "Ander", spesifiseer asseblief: _____

4. Wat is die hoogste standerd (graad) wat jy behaal het?

_____

5. Het jy enige na-skoolse kwalifikasies?

Ja	1
Nee	2

Indien "Ja", spesifiseer asseblief: _____

6. Wat is jou huistaal?

Engels	1
Khosa	2
Afrikaans	3
Ander	4

Indien "Ander", spesifiseer asseblief: _____

7. Is jy?

Enkellopend	1
Getroud of woon saam met besondere ander	2
Vervreem, geskei, weduwee/wewenaar	3

8. Verdien jy 'n inkomste buite die huis?

Ja	1
Nee	2

9. Wat is jou huishoudelike inkomste?

R0- R500	1
R501- R1000	2
R1001- R2000	3
R2001- R5000	4
R5001- R8000	5
R8001- R10000	6
Meer as R10000	7

10. Neem jy op die huidige oomblik voorgeskrewe medikasie vir enige van die volgende?

	Ja	Nee
1. Psigiatriese probleme (bv. Vir jou senuwees)	1	2
2. Hoë bloeddruk	1	2
3. Suiker	1	2
4. Arthritis/rheumatiek	1	2
5. Tuberkulose/TB	1	2
6. Kanker	1	2
7. Ander (spesifiseer asseblief_____)	1	2

11. Het jy jou dokter besoek gedurende die afgelope 6 maande vir MIV/VIGS behandeling?

Ja	1
Nee	2

Indien "Ja", hoeveel keer het jy jou dokter besoek?

1 - 2 keer	1
3 - 4 keer	2
Meer as 4 keer	3

Instruksies: Antwoord asseblief die volgende vrae deur die nodige blokkie te merk " /".

B: Die volgende afdeling verwys na die neem van MIV/VIGS medikasie:

Kies asseblief een blokkie vir elke vraag (kies een)

	Glad nie seker nie	Seker	Baie seker	Geheel en al seker
1. Hoe seker is jy dat jy die meeste of al jou medisyne sal kan neem?	0	1	2	3
2. Hoe seker is jy dat the MIV/VIGS medikasie 'n positiewe effek op jou gesondheid sal hê?	0	1	2	3
3. Hoe seker is jy, dat as jy nie jou MIV medikasie sou neem soos aangewys nie, die MIV in jou liggaam bestand sal raak teen die MIV medisyne.	0	1	2	3

C: Die volgende vrae verwys na jou ondersteunings netwerk:

Kies asseblief een blokkie vir elke vraag (kies een)

	Baie Ontevrede	Ontevrede	Tevrede	Baie Tevrede
1. In die algemeen, hoe tevrede is jy oor die algehele ondersteuning van jou vriende of familielede?	0	1	2	3

	Glad Nie	Baie Min	n Bietjie	Baie	Nut
2. Tot watter mate help jou vriende of familie lede jou om te onthou om jou medikasie te neem?	0	1	2	3	4

D: Mense mag om verskeie redes vergeet om hulle MIV medikasie te neem. Hier is 'n lys van redes waarom jy mag vergeet om jou medikasie te neem.

Gedurende die afgelope maand, hoe gereeld het jy vergeet om jou medikasie te neem a.g.v. die volgende redes? Kies asseblief een blokkie vir elke vraag (kies een)

	Nooit	Min	Soms	Gereeld
1. Jy was nie by die huis nie?	0	1	2	3
2. Jy was besig met ander dinge?	0	1	2	3
3. Jy het eenvoudig vergeet?	0	1	2	3
4. Jy het te veel pille/tablette gehad om te neem?	0	1	2	3
5. Jy wou nie die newe- effekte beleef het nie?	0	1	2	3
6. Jy wou nie hê dat ander moet sien dat jy medikasie neem nie?	0	1	2	3
7. Daar was 'n verandering in jou daaglikse roetiene?	0	1	2	3
8. Jy het gevoel dat die medikase giftig was vir jou sisteem?	0	1	2	3
9. Jy het geslaap tydens dosistyd?	0	1	2	3
10. Jy het siek gevoel?	0	1	2	3
11. Jy was depresief/ neerslagtig?	0	1	2	3
12. Jy het dit moeilik gevind om die medikasie tydens gespesifiseerde tye te neem (met maaltye, op 'n leë maag, ens)?	0	1	2	3
13. Jy het geen pille oor gehad nie/ Jou pille was op?	0	1	2	3
14. Jy het goed gevoel?	0	1	2	3

Instruksies: Antwoord asseblief die volgende vrae deur die nodige blokkie te merk " /".

E: Die volgende afdeling verwys na die hoeveelheid en gereeldheid waarmee jy jou MIV medikasie moet neem.

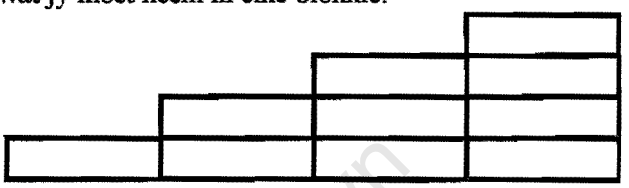
1. Jy moet jou pille neem: (Kies een)

Een maal per dag	1
Twee maal per dag	2
Drie maal per dag	3
Vier maal per dag	4

2. Hoeveel pille moet jy neem vir elke dosis?

Skryf asseblief die hoeveelheid pille wat jy moet neem in elke blokkie.

Een maal per dag
Twee maal per dag
Drie maal per dag
Vier maal per dag



F: Die volgende afdeling verwys na die hoeveelheid kere jy vergeet het om jou MIV medikasie te neem gedurende die afgelope 4 dae.

Indien jy slegs 'n gedeelte van 'n dosis geneem het op een of meer van die dae, meld asseblief dat die dosis nie geneem is nie.

1. Gedurende die afgelope vier dae, hoeveel dae her jy vergeet om jou dosis te neem?

(Kies een)

Geen	0
Een dag	1
Twee dae	2
Drie dae	3
Vier dae	4

G: Die meeste MIV medikasies moet volgens 'n skedule geneem word, bv. een maal per dag, twee maal per dag of elke 8 ure?

1. Gedurende die afgelope 4 dae, hoe streng het jy die instruksies gevolg? (Kies een)

Nooit	0
Soms	1
Helfte van die tyd	2
Meeste van die tyd	3
Al die tyd	4

H: Het enige van jou MIV medikasie spesifieke instruksies soos byvoorbeeld, "neem met maaltye", "moenie neem tydens maaltye nie" of "neem met baie vloeistowwe"?

(Kies een)

Ja	0
Nee	1

Indien "Ja", hoe streng het jy die instrusies gevolg gedurende die afgelope 4 dae?

(kies een)

Nooit	0
Soms	1
Helfte van die tyd	2
Meeste van die tyd	3
Al die tyd	4

I: Sommige mense vergeet om hulle MIV medikasie te neem oor naweke. Het jy vergeet om jou medikasie te neem gedurende die afgelope naweek?

(kies een)

Ja	0
Nee	1

J: Wanneer was die laaste keer wat jy vegeet het om jou MIV medikasie te neem?

(kies een)

Gedurende die afgelope week	5
1-2 weke gelede	4
2-4 weke gelede	3
1-3 maande gelede	2
Meer as 3 maande gelede	1
Ek vergeet nooit	0

K: Die volgende afdeling verwys na jou emosionele toestand / hoe jy voel.

Kies asseblief een blokkie vir elke vraag. (kies een)

	Nooit Min	Soms	Gereeld	Meeste van die tyd
1. Gedurende die afgelope week, hoeveel keer het jy afgemat gevoel en kon jy nie die gevoel afskud nie, selfs met die help van jou vriende of familie?	0	1	2	3
2. Gedurende die afgelope week, hoeveel keer het jy gevoel asof jy nie kon konsentreer op waarmee jy besig was nie?	0	1	2	3
3. Gedurende die afgelope week, hoeveel keer het jy gevoel dat alles wat jy doen baie moeite verg?	0	1	2	3
4. Gedurende die afgelope week, hoeveel keer het jy dit moeilik gevind om te slaap?	0	1	2	3
5. Gedurende die afgelope week, hoeveel keer het jy alleen gevoel?	0	1	2	3
6. Gedurende die afgelope week, hoeveel keer het jy hartseer gevoel?	0	1	2	3
7. Gedurende die afgelope week, hoeveel keer het jy gevoel dat jy nie aan die gang kon kom nie?	0	1	2	3

L: Gedurende die afgelope maand, hoe gereeld;

Kies asseblief een blokkie vir elke vraag. (kies een)

	Nooit	Amper Nooit	Soms	Gereeld	Amper Altyd
1. Was jy ongelukkig omdat iets onverwags gebeur het?	0	1	2	3	4
2. Het jy gevoel asof dit ontmoontlik was om beheer te kry oor die belangrike dinge in jou lewe?	0	1	2	3	4

L: (Vervolg) Gedurende die afgelope maand, hoe gereeld;

Kies asseblief een blokkie vir elke vraag. (kies een)

	Nooit	Amper Nooit	Soms	Gereeld	Amper Altyd
3. Was jy senuweeagtig of gestres?	0	1	2	3	4
4. Het jy selfversekerd gevoel in jou vermoë om jou persoonlike probleme uit te sorteer?	0	1	2	3	4
5. Het jy gevoel asof dinge in jou guns was?	0	1	2	3	4
6. Het jy gevoel dat jy nie alles wat jy moes doen, kon behartig nie?	0	1	2	3	4
7. Kon jy die irritasies in jou lewe hanteer?	0	1	2	3	4
8. Het jy gevoel asof jy alles onder beheer gehad het?	0	1	2	3	4
9. Was jy kwaad omdat dinge wat gebeur het, buite jou beheer was?	0	1	2	3	4
10. Het jy gevoel dat dinge te veel geraak het vir jou?	0	1	2	3	4

M: Gesondheidsgedrag verskil tussen mense. Die volgende vrae verwys na jou alkohol en dwelmgebruik huidiglik en in die verlede.

1. Gedurende die afgelope 30 dae, hoe gereeld het jy 'n drankie grdrink ('n glas bier, 'n glas wyn, 'n gemengde drankie of enige iets alkoholies)?

(kies een)

Daagliks	6
Amper elke dag	5
1 - 2 maal per week	4
3 - 4 maal per week	3
2 - 3 maal per maand	2
Een maal per maand	1
Nooit	0

Indien "Nooit" - gaan asseblief na vraag 4.

2. Gedurende die afgelope 30 dae, hoeveel drankies het jy gedrink per dag? 'n Drankie verwys na 'n blikkie of 'n glas bier, 'n glas wyn, of 'n gemengde drankie (vb brandewyn en coke)

(kies een)

1 - 2 drankies per dag	0
3 - 4 drankies per dag	1
5 - 6 drankies per dag	2
7 - 8 drankies per dag	3
9 - 11 drankies per dag	4
12 of meer drankies per dag	5

3. Gedurende die afgelope 30 dae, hoeveel keer het jy vyf of meer drankies namekaar gehad? (bv. binne 2 - 4 ure)

(kies een)

Daagliks	6
Amper elke dag	5
1 - 2 maal per week	4
3 - 4 maal per week	3
2 - 3 maal per maand	2
Een maal per maand	1
Nooit	0

4. Merk asseblief "Ja" of "Nee" vir elk van die volgende vrae.

a. Het jy ooit vantevore dagga/marajiuana gebruik?

Ja	1
Nee	2

Indien "Ja", het jy dit gedurende die afgelope 6 maande gebruik?

Ja	1
Nee	2

b. Het jy ooit vantevore mandrax/buttons gebruik?

Ja	1
Nee	2

Indien "Ja", het jy dit gedurende die afgelope 6 maande gebruik?

Ja	1
Nee	2

c. Het jy ooit vantevore heroiene gebruik?

Ja	1
Nee	2

Indien "Ja", het jy dit gedurende die afgelope 6 maande gebruik?

Ja	1
Nee	2

d. Het jy ooit vantevore amfetamiene (speed) gebruik?

Ja	1
Nee	2

Indien "Ja", het jy dit gedurende die afgelope 6 maande gebruik?

Ja	1
Nee	2

e. Het jy ooit vantevore kokaiene (coke/crack/freebase) gebruik?

Ja	1
Nee	2

Indien "Ja", het jy dit gedurende die afgelope 6 maande gebruik?

Ja	1
Nee	2

f. Het jy ooit vantevore ecstacy ("e") gebruik?

Ja	1
Nee	2

Indien "Ja", het jy dit gedurende die afgelope 6 maande gebruik?

Ja	1
Nee	2

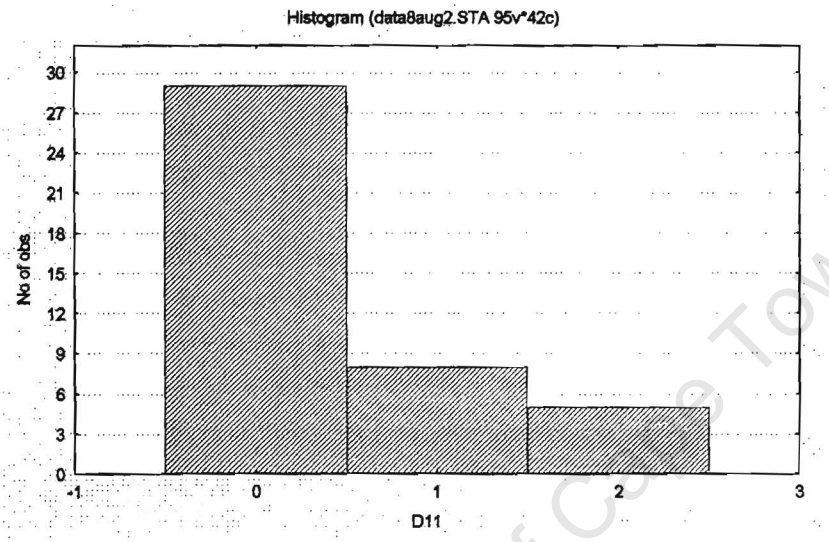
Dankie vir jou samewerking.

Dankie dat jy die tyd geneem het on die vrae te beantwoord. Ons waardeer jou bydrae.

Appendix 6: Histograms of reasons for missed doses

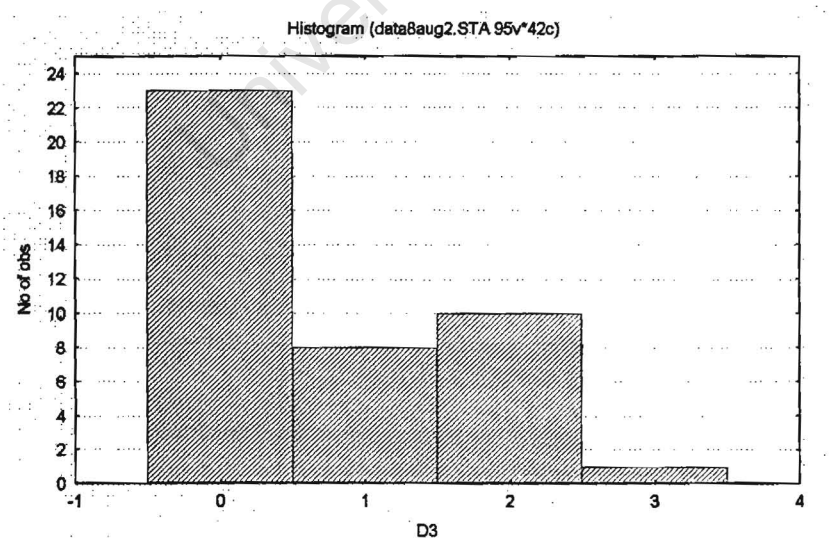
In the figures below the numbers of participants recording various reasons for missing doses are shown. Legend for all the histograms: 0= never; 1= rarely; 2= sometimes; 3= often. In order to rank these responses 1, 2 and 3 were added to give a sum of the number of participants who had responded affirmatively. Ranking 1= most used reason etc.

Figure 1: Responses to section D question 11 (You felt depressed/overwhelmed?).



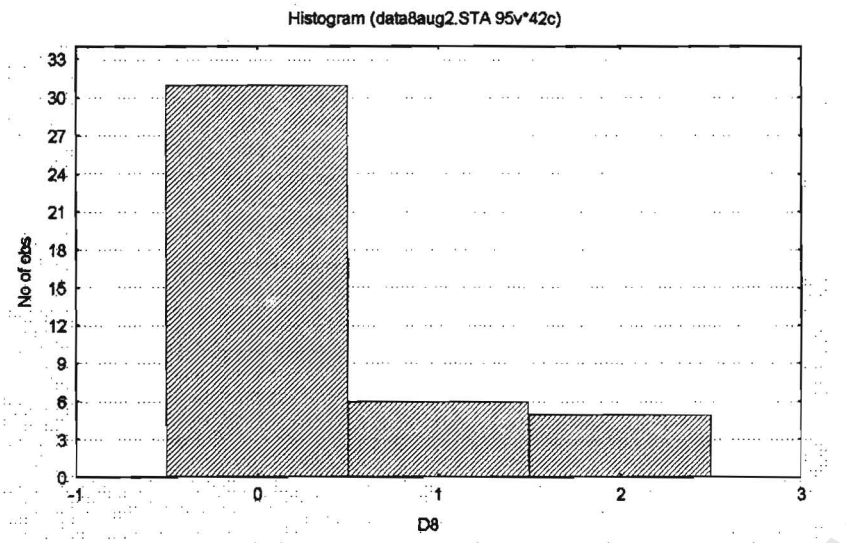
Ranking 1

Figure 2: Responses to section D question 3 (You simply forgot?)



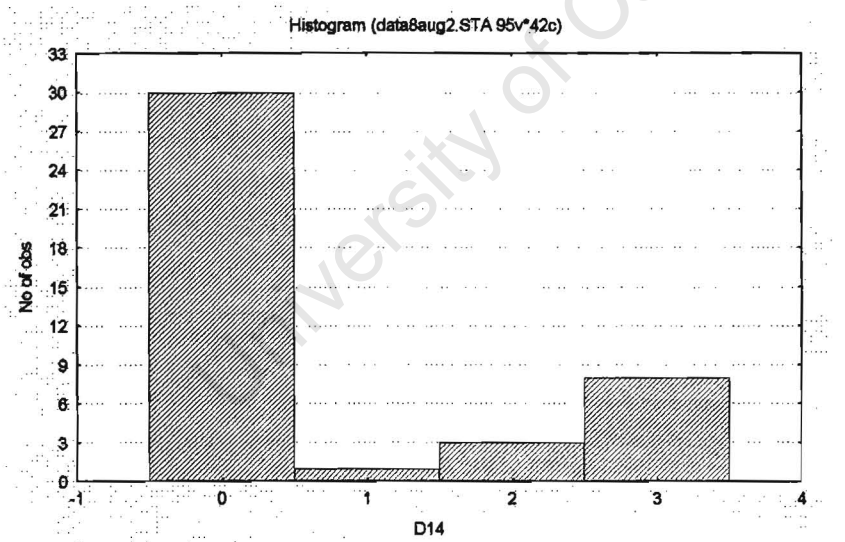
Ranking 2

Figure 3: Responses to section D question 8 (You felt like the drug was toxic/harmful?)



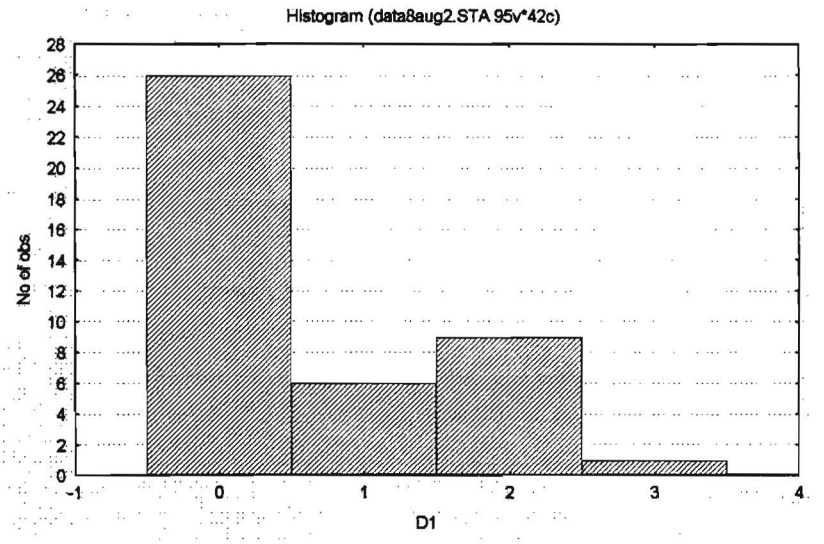
Ranking 2

Figure 4: Responses to section D question 14 (You felt good?).



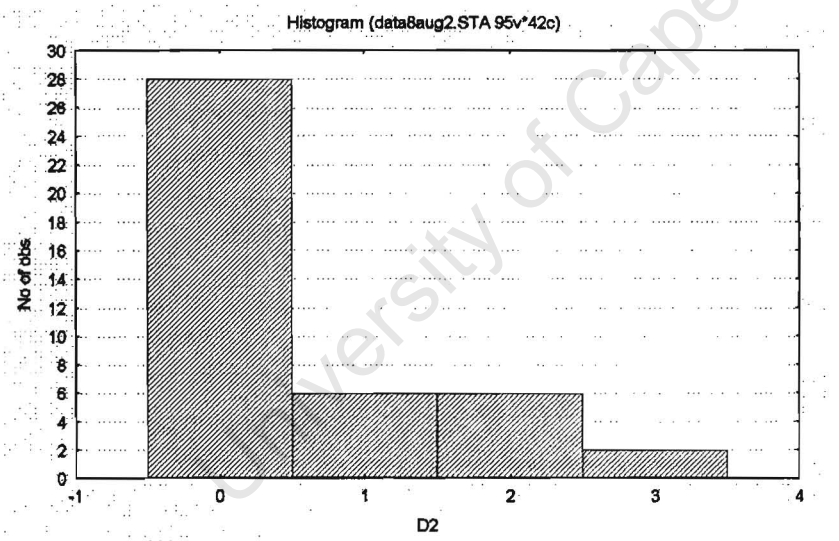
Ranking 2

Figure 5: Responses to section D question 1 (You were away from home?)



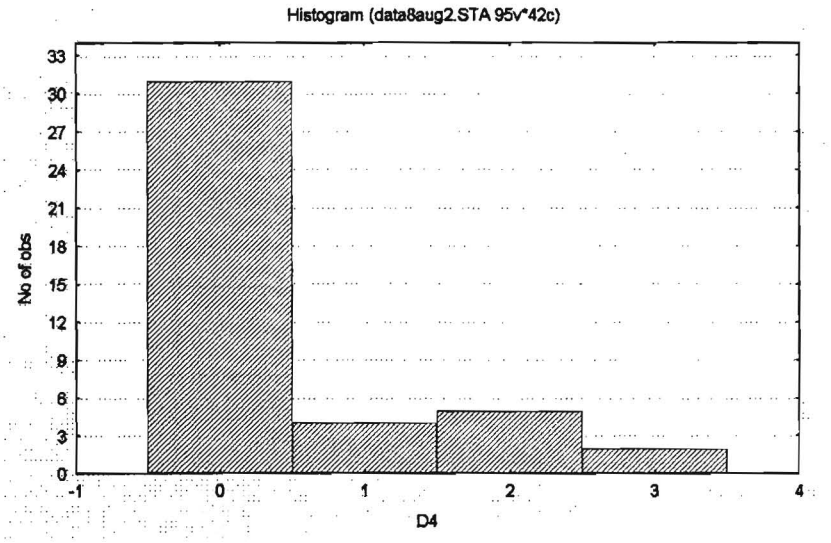
Ranking 3

Figure 6: Responses to section D question 2 (You were busy with other things?)



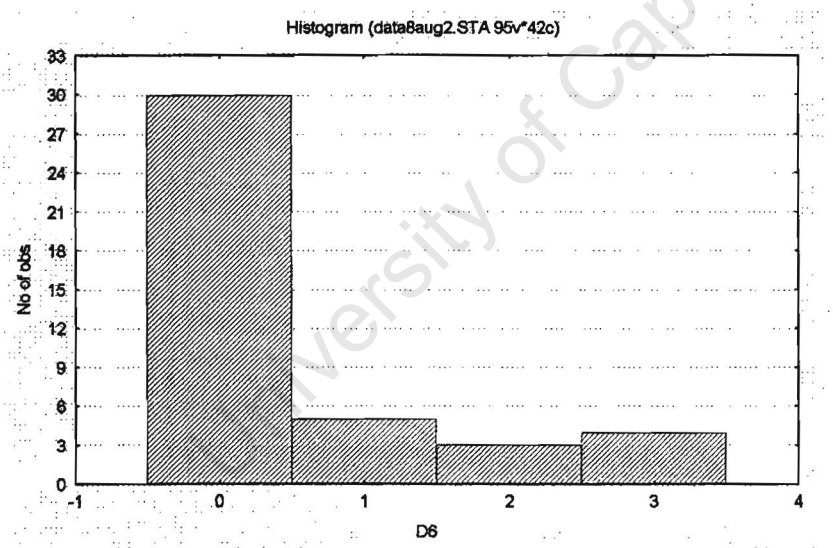
Ranking 4

Figure 7: Responses to section D question 4 (You had too many pills/tablets to take?)



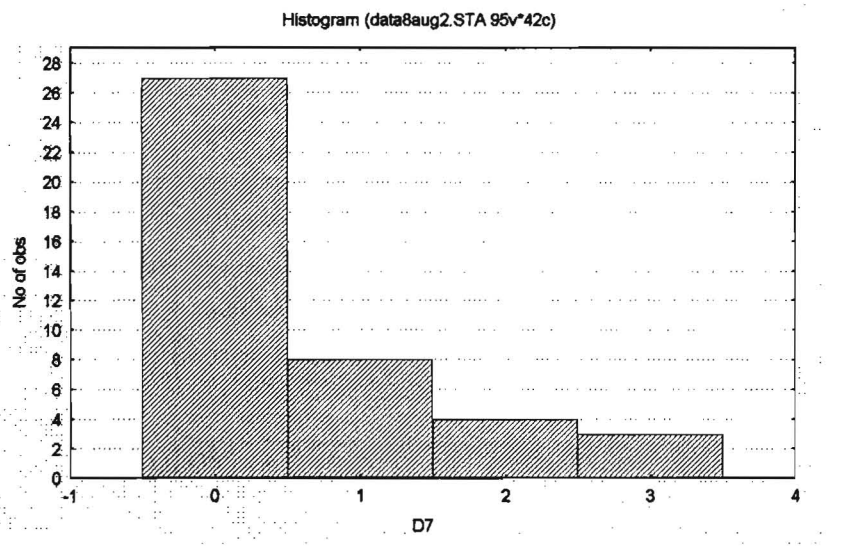
Ranking 5

Figure 8: Responses to section D question 6 (You did not want others to notice you taking medication?)



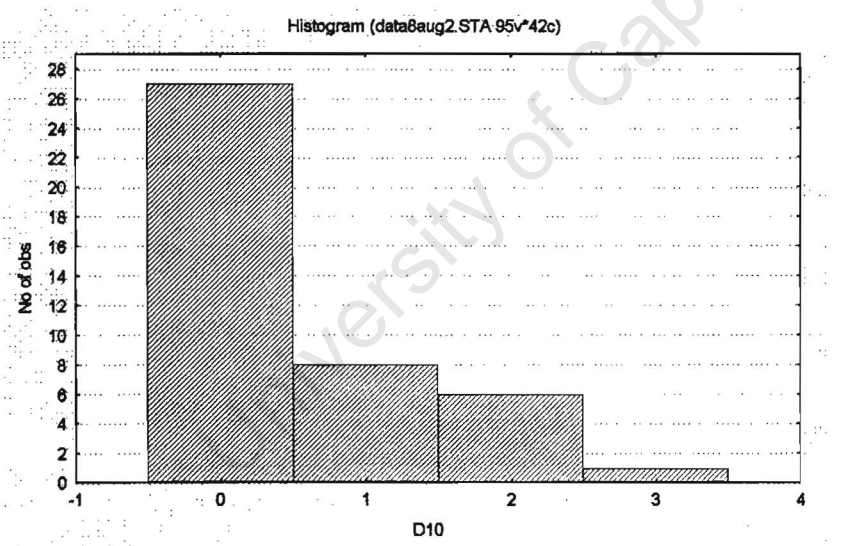
Ranking 5

Figure 9: Responses to section D question 7 (You had a change in your daily routine?)



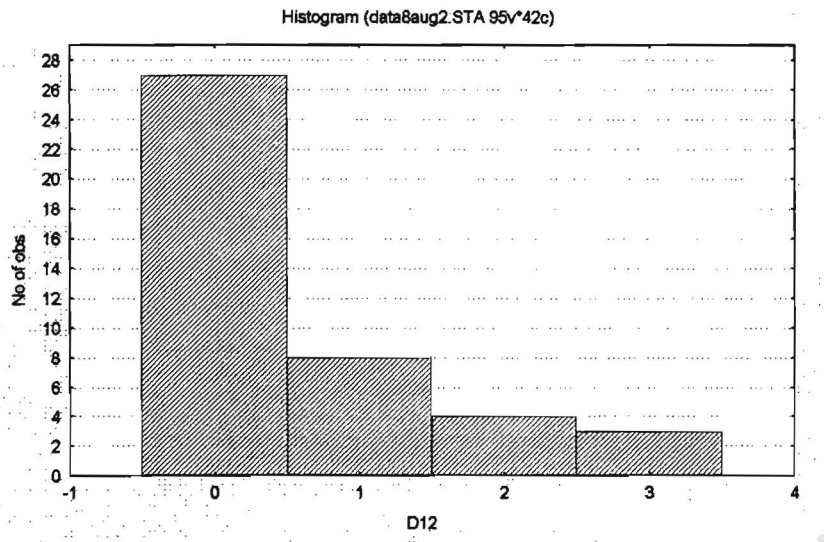
Ranking 5

Figure 10: Responses to section D question 10 (You felt sick or ill?)



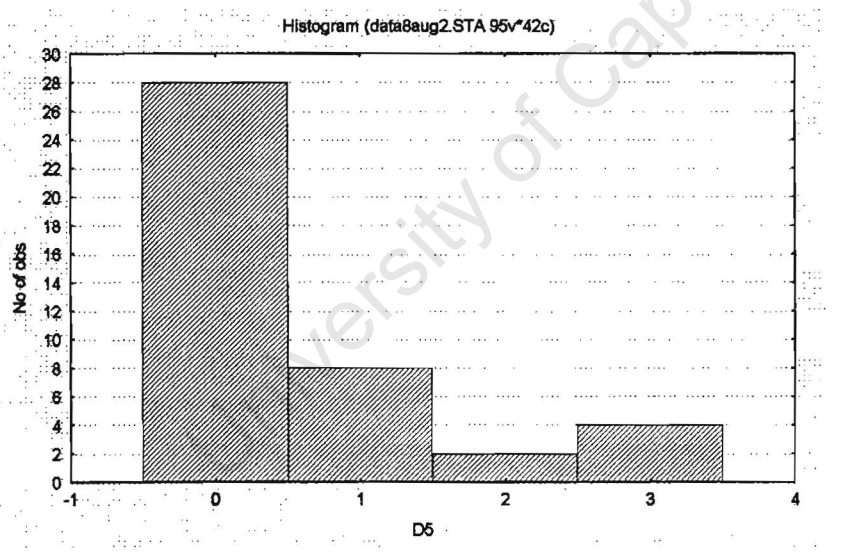
Ranking 5

Figure 11: Responses to section D question 11 (You had problems taking the pills/tablets at specified times (with meals, on empty stomach, etc)?



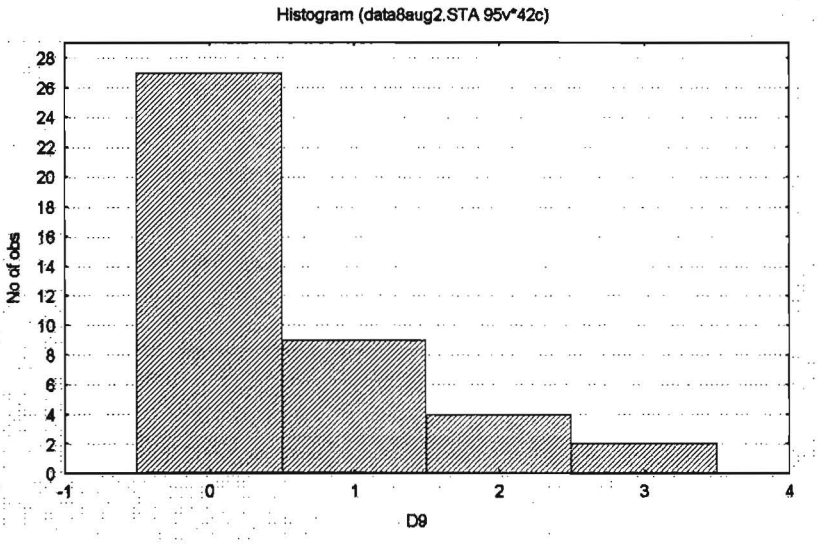
Ranking 5

Figure 12: Responses to section D question 5 (You wanted to avoid side effects?)



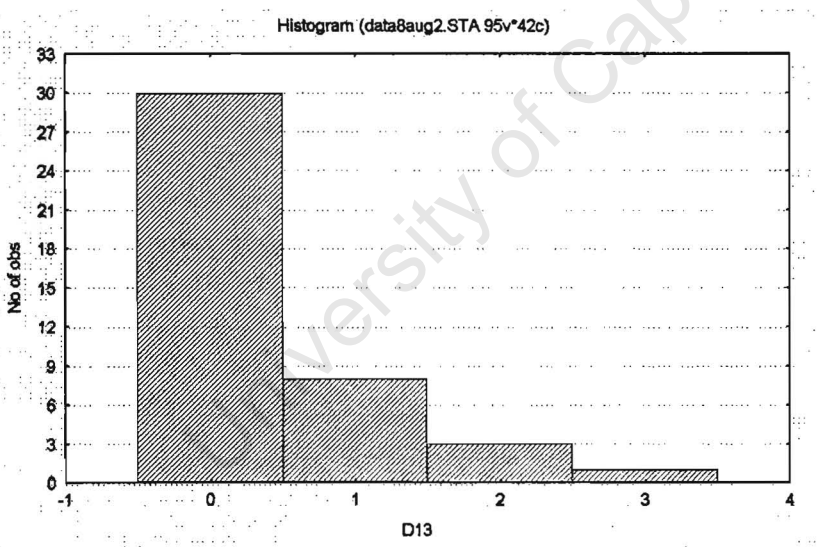
Ranking 6

Figure 13: Responses to section D question 9 (You fell asleep/slept through the dose time?)



Ranking 6

Figure 14: Responses to section D question 13 (You ran out of pills/tablets?)



Ranking 7